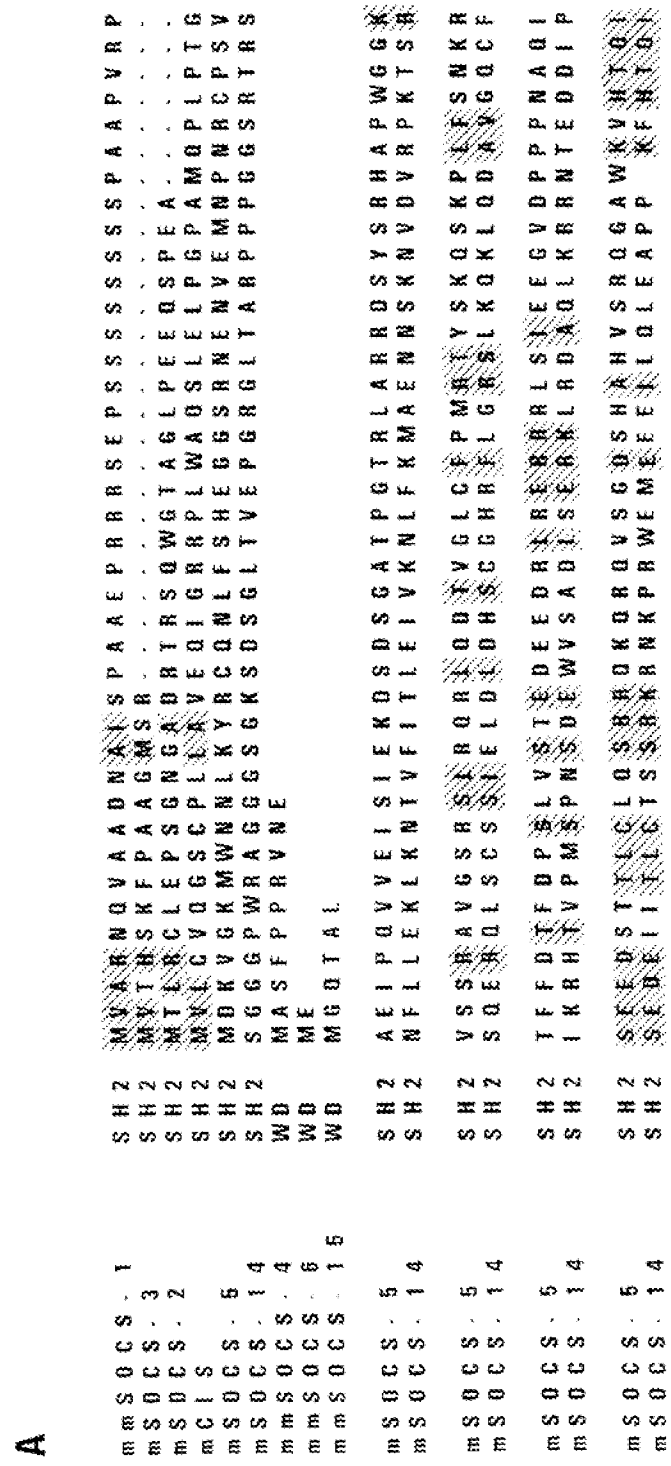

A
mmSOCS-1 SH2 MVARNQVAADNALSPAAEPRRRSEPSSSSSSSSSSPAAPVRP
mmSOCS-3 SH2 MFTHSKFPAAGMSR.....PEEQSPEA.....
mmSOCS-2 SH2 MNTERCLEPSGNGADRTRSQWGTAGLPEEQSPEA.....
mmCLS-5 SH2 MNLCVQGSCPLLKVEQIGRRPLWAQSSLELPGPAMQPLPTG
mmSOCS-1 SH2 MDKVGKMWNWLKYRCQWLFSHEGGSRKENVEMNPWRCPSV
mmSOCS-4 SH2 SGGGPWRAGGSGKSDSGLTVEPGRGLTARPPPGGSRTRS
mmSOCS-6 WD MASFPPRVWE
mmSOCS-15 WD ME
mmSOCS WD MGDTAL
mmSOCS-5 SH2 AEIPQVVEISLEKDSDSGATPGTRLARRQDSYSRHAPWGGK
mmSOCS-14 SH2 NFLLEKLKNTVFITLEIVKNLFKMAENNSKNVDVRPKTSR
mmSOCS-5 SH2 VSSRAVGSRSLRQRAQDFVGLCPMRTYSKQSKPLFSWKR
mmSOCS-14 SH2 SQEHQLSCSSLEELDYDHSCGHRFLGRSLKQKLQDAPGQCF
mmSOCS-5 SH2 TFFDTFDPSLVSTFDEEDRLREERRLSLEEGVDPPPNAQI
mmSOCS-14 SH2 IKRHTVPMSPMSDEWVSADISERKLRDAQLKRRNTEDDIP
mmSOCS-5 SH2 SKEDSTFLGLQSRRQKQRQVSGQSHAHVSRQGAWKVHTQI
mmSOCS-14 SH2 SEDEIIFLGTSSRKRNKPRWEMEELLQLEAPP KFHTQI

FIG. 13 A (ii)

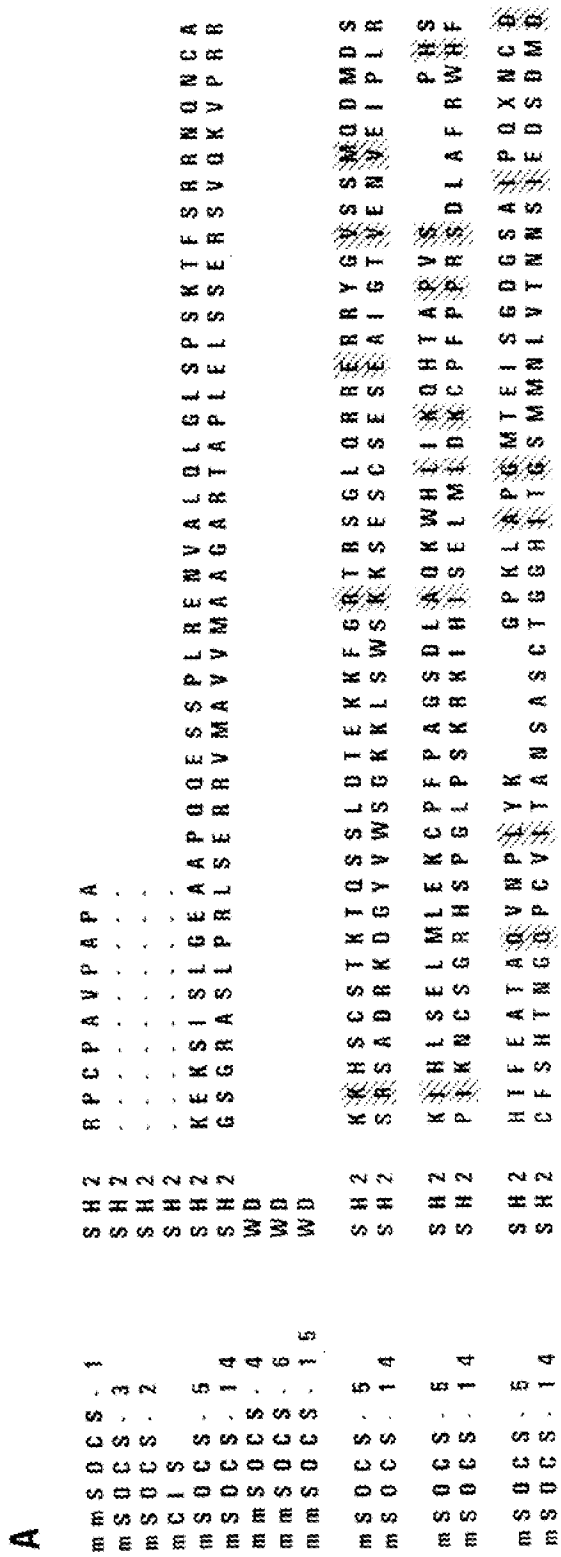

A
mmSOCS-1 SH2 RPCPAVPAPA
mmSOCS-3 SH2 . . . . . .
mmSOCS-2 SH2 . . . . . .
mmCIS SH2 . . . . . .
mmSOCS-5 SH2 KEKSISLGEAAPQQESSPLREMVALQLGLSPSKTFSRRMQNCA
mmSOCS-14 SH2 GSGRASLPRLSERRVMAVVMAAGARTAPLELSSERSVQKVPRR
mmSOCS-4 WD
mmSOCS-6 WD
mmSOCS-15 WD
mSOCS-5 SH2 KKHSCSTKTQSSLDTEKKFGRTRSGLQRREERRYGYSSSMQDMDS
mSOCS-14 SH2 SRSSADRKDGYVWSGKKLSWSKKSESCSESEAIGTYEMYEIPLR
mSOCS-5 SH2 KYHLSELMLEKCPFPAGSDLAQKWHLIKQHTAPVSPWS
mSOCS-14 SH2 PYKNCSGRHSPGLPSKRKHISELMEDKCPFPRSDLAFRWHF
mSOCS-5 SH2 HIFEATAQVMPLYK GPKLAPGMTEISGDGSAPQYXNCQ
mSOCS-14 SH2 CFSHTMGQPCVSTAWSASCTGSHTIGSMMNLVTMNSEDSDMD
mSOCS-5 SH2 DYLHCLVPDLLQLTGMP
mSOCS-14 SH2 DYVHCLVPDLLQISNMP

FIG. 13 A (ii)

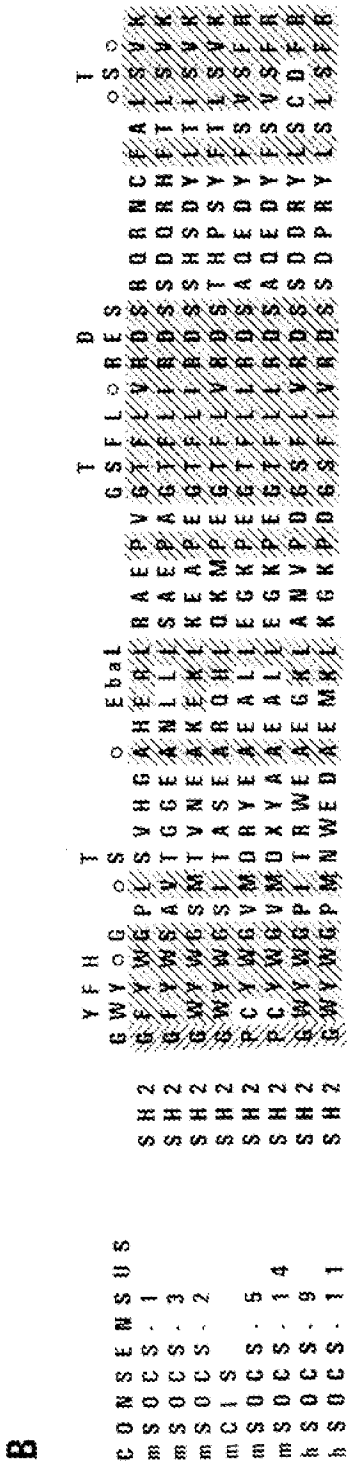

B
CONSENSUS
mSOCS-1
mSOCS-3
mSOCS-2
mCLSOCS-5
mSOCS-14
mSOCS-9
hSOCS-11
SH2
YFH T
GWYOG oS
GEYWEPLSVHGAHEALI
GEYWSAVTGGEAWLLI
GEYWGSMTVNEAKEKI
GEYWGSLTASEARQHL
GEYWGVMDRYEWEALL
PCYWGVMDKYAWEALL
PCYWGPLIRWEAEGKL
GVWGPMNWEDKEMKLK
Ebal
SAEPAVGTFLVRDSSDQRHFILSVK
SAEPAAGTFLIRDSSHSDYIISVK
KEAPEGTFLVRDSSTHPSYFILSVK
DKMPEGTFLLRDSSAQEDYFSVSFR
EGKPEGTFLLRDSSAQEDYFSVSFR
EGKPEGTFLVRDSSDDRYLSCDFR
ANVPDGSFLVRDSSDPRYLSLSFR
KGKPDGSFLVRDSSDPRYLSLSFR
T
D
OSO

FIG. 13 B (ii)

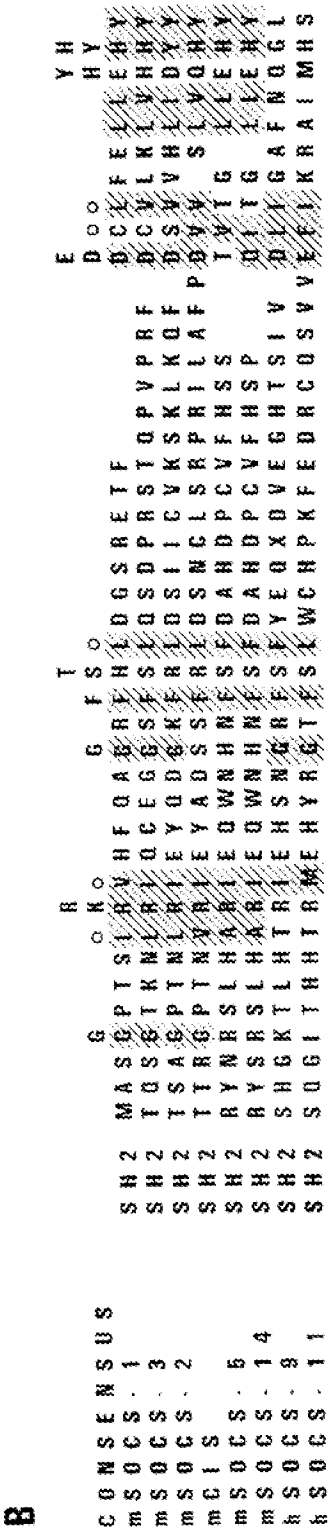


FIG. 13 B (iii)

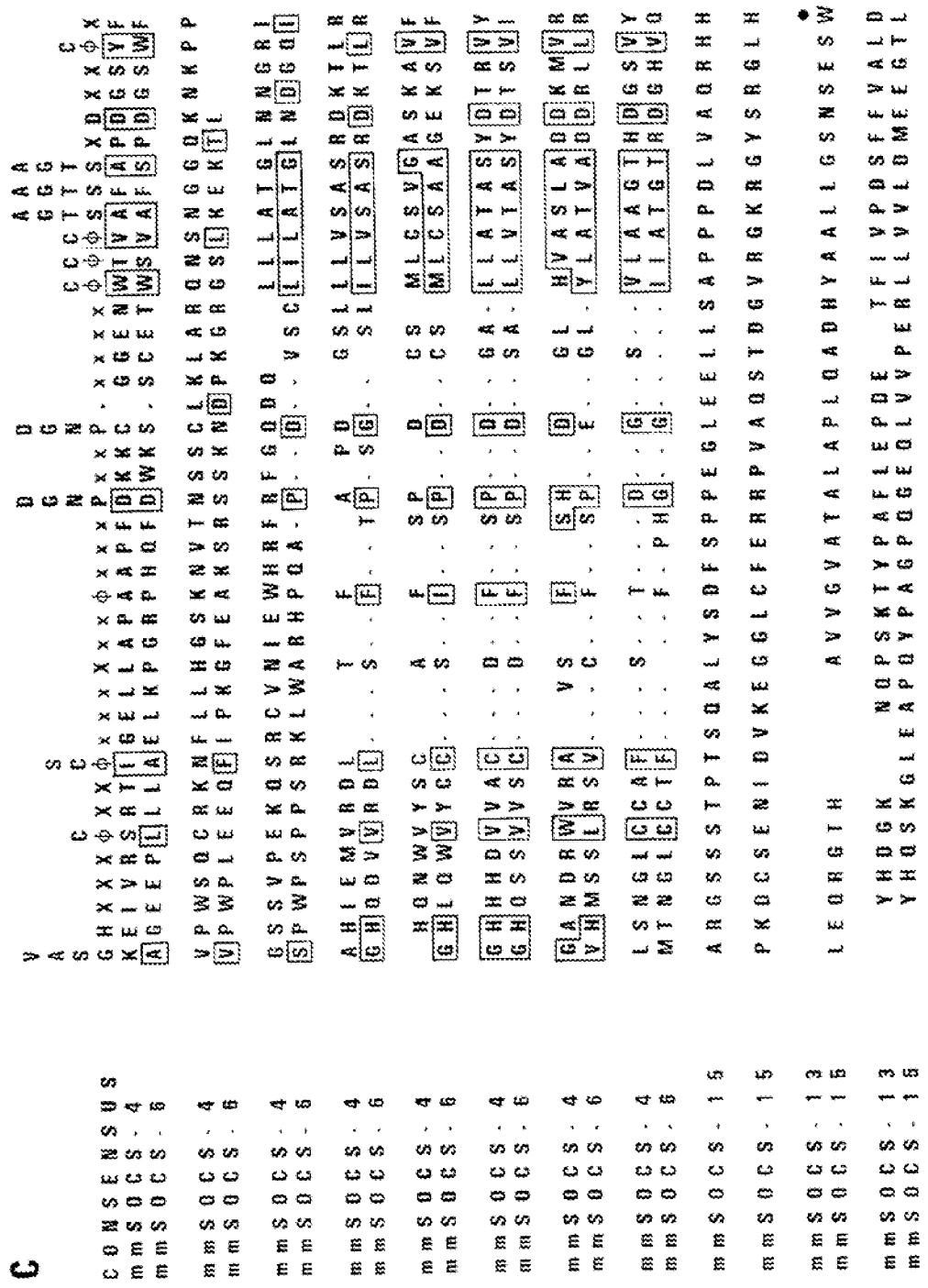


FIG. 13 C (ii)

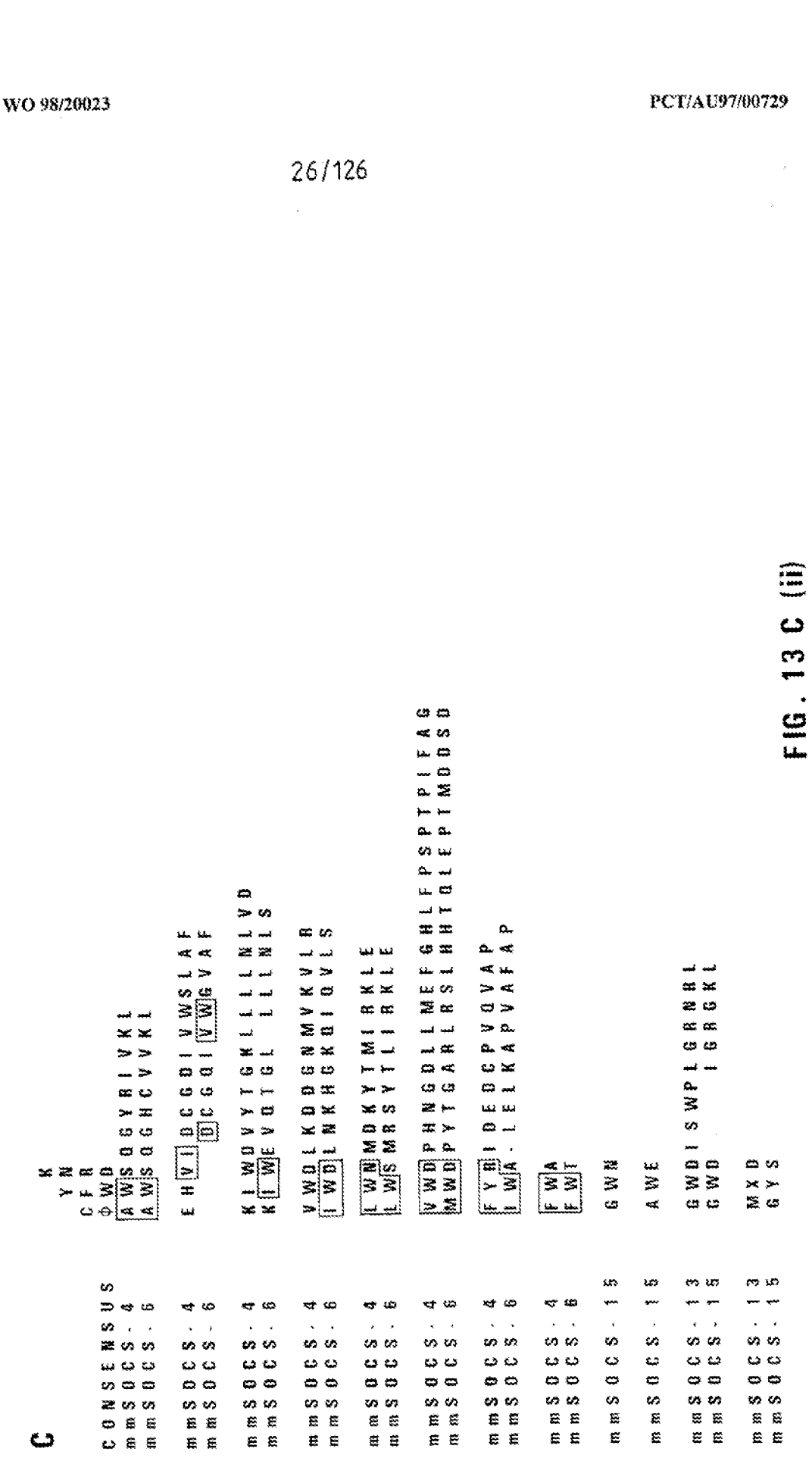

C
CONSENSUS
mmSOCS-4
mmSOCS-6
mmSOCS-4
mmSOCS-6
mmSOCS-4
mmSOCS-6
mmSOCS-4
mmSOCS-6
mmSOCS-4
mmSOCS-6
mmSOCS-4
mmSOCS-6
mmSOCS-4
mmSOCS-6
mmSOCS-15
mmSOCS-15
mmSOCS-13
mmSOCS-15
mmSOCS-13
mmSOCS-15

FIG. 13 C (iii)

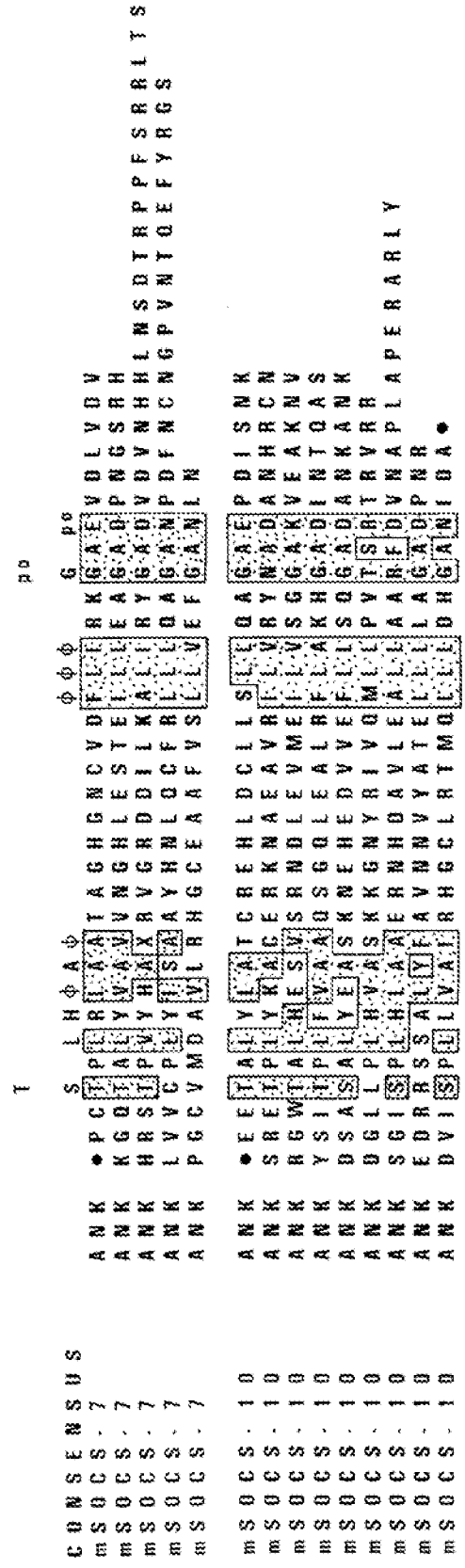


FIG. 13 D

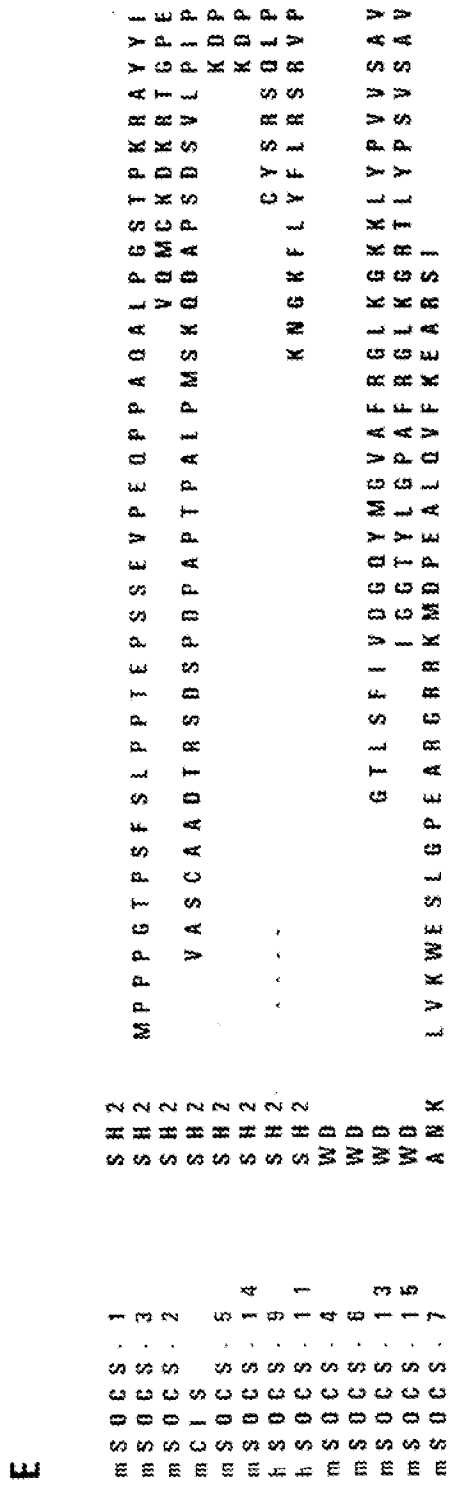

E
mSOCS-1
mSOCS-3
mSOCS-2
mCISS-5
mSOCS-14
mSOCS-9
hSOCS-11
hSOCS-4
mSOCS-6
mSOCS-13
mSOCS-15
mSOCS-7
SH2
SH2
SH2
SH2
SH2
SH2
SH2
WD
WD
WD
WD
ANK
MPPPGTPSFSLPPTEPSSEVPEQPPAQALPGSTPKRAYYI
VASCAADTRSDSPDPAPTPALPMSKQQDAPSDSVLPIPKDP
KNGKFLYFLRSRVP
CYSRSSQLP
VQQMCKDKRTGPE
GTLSFIVQGQYMGVAFRGLKGKKLYPVVSAV
IGGTYLGPAFRGLKGRTLYPSVSAV
LVKWESLGPEARGRRKMDPEALQVFKEARSI

FIG. 13 E (i)

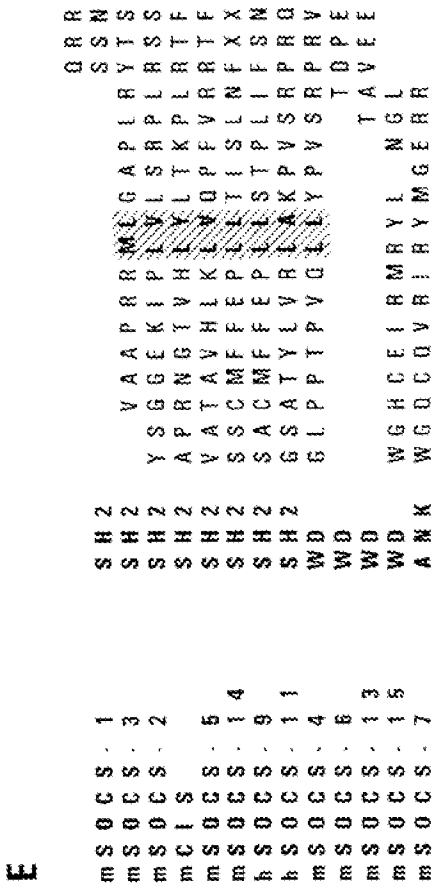


FIG. 13 E (iii)

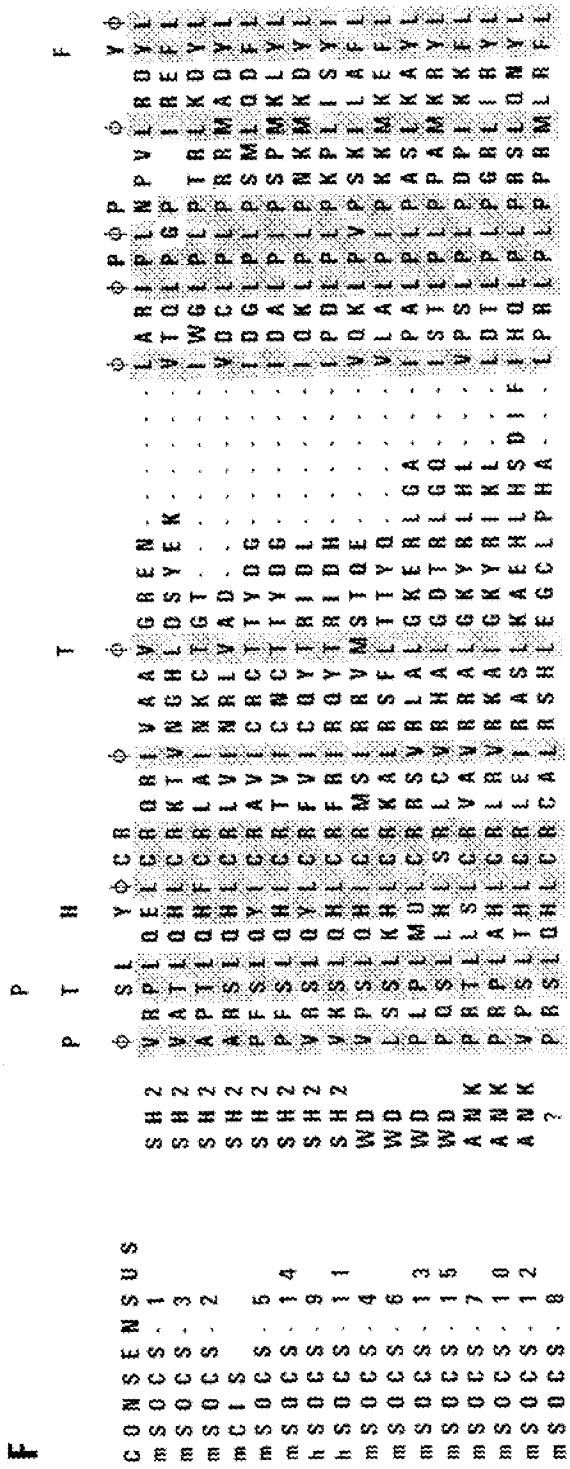


FIG. 13 F (i)

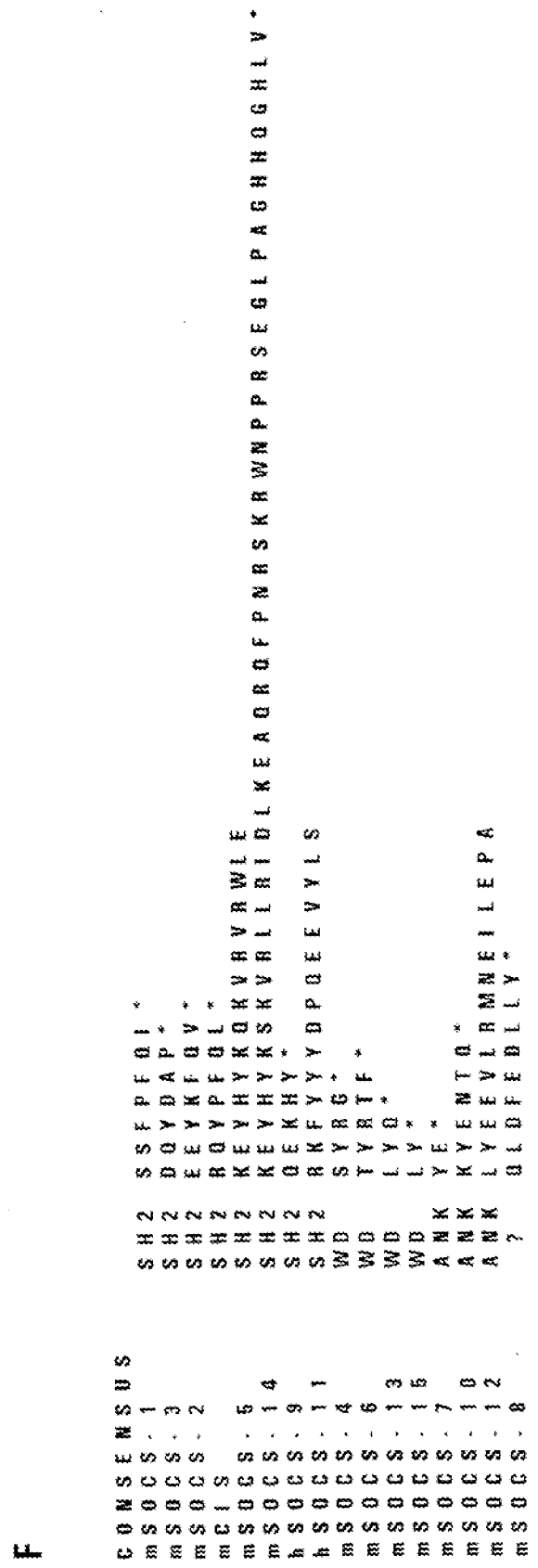

F
consensus
mssocss.1
mssocss.3
mssocss.2
mscLss.5
mssocss.14
mssocss.9
hssocss.11
hssocss.4
mssocss.6
mssocss.13
mssocss.15
mssocss.7
mssocss.10
mssocss.12
mssocs.8
SH2 SSEPFQL*
SH2 DQYDAP*
SH2 EEYKFQV*
SH2 RQYPFQL*
SH2 KEYHYYKQKVRVRWLE
SH2 KEYHYKSKVRLLRIQLKEAQRQFPNRSKRWNPPRSEGLPAGHHQGHLV*
SH2 QEKHY* PQEEVYLS
SH2 RKFYYYDPQEEVYLS
WD SYRG* *
WD TYRTF*
WD LYQ*
WD LY* *
ANK KYE* NTQ*
ANK KYEEVLRMNEILEPA
ANK QLQFEDLLY*
?

FIG. 13 F (iii)

FIG 14A

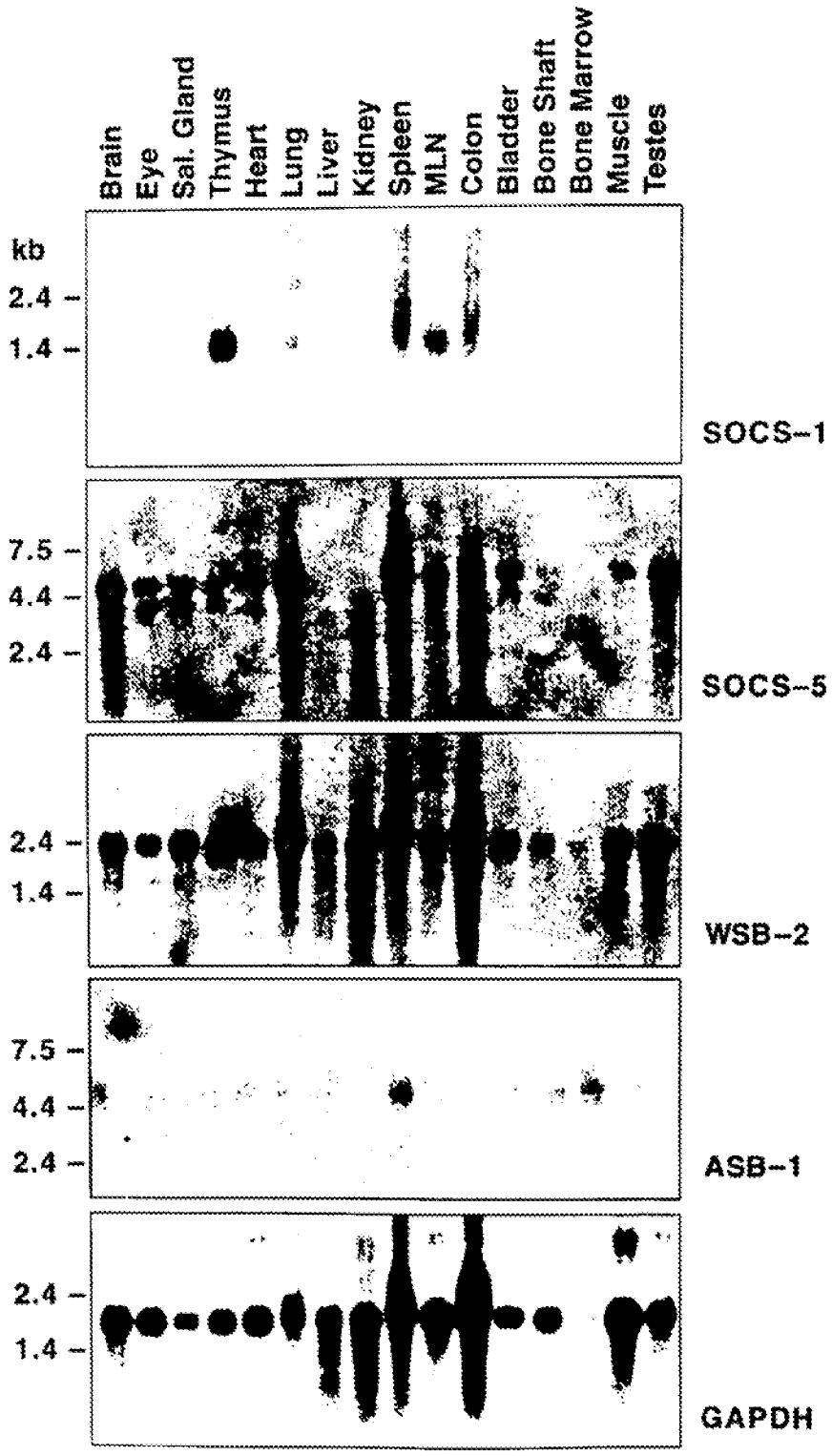
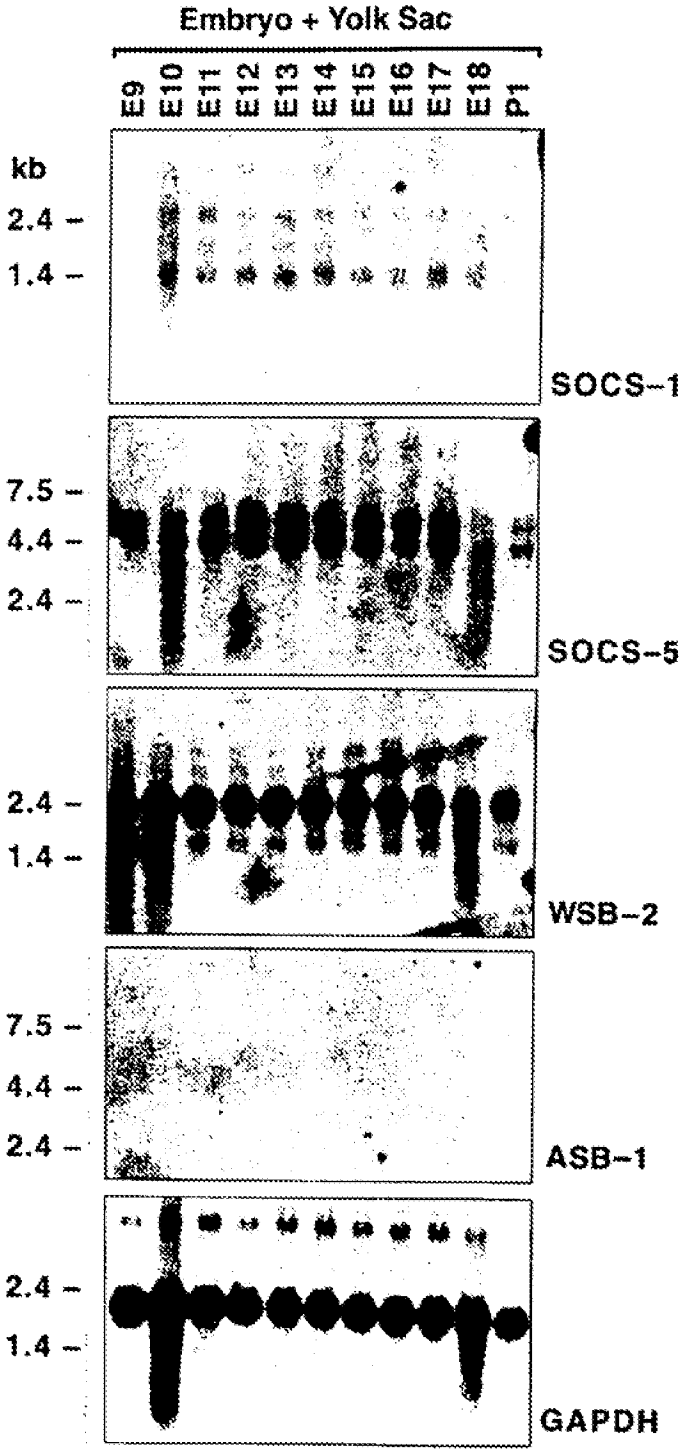

Brain
Eye
Sal. Gland
Thymus
Heart
Lung
Liver
Kidney
Spleen
MLN
Colon
Bladder
Bone Shaft
Bone Marrow
Muscle
Testes
kb
2.4
1.4
SOCS-1
7.5
4.4
2.4
SOCS-5
2.4
1.4
WSB-2
7.5
4.4
2.4
ASB-1
2.4
1.4
GAPDH

FIG 14B


Embryo + Yolk Sac
E9
E10
E11
E12
E13
E14
E15
E16
E17
E18
P1
kb
2.4
1.4
SOCS-1
7.5
4.4
2.4
SOCS-5
2.4
1.4
WSB-2
7.5
4.4
2.4
ASB-1
2.4
1.4
GAPDH

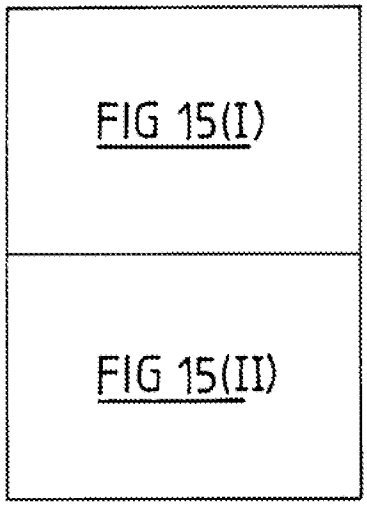


FIG 15

cgaattccgggcgggctgtgtgagtctgtgagtggaaggcgccggcctctttgtct
gagtgtgaccccggtggcttttgttccaggcattccctccggtgatttcctccgggcagtccgc
agaagccgcagcggccgccgctctctctgcagtctccacacccgggagagcctga
gcccgcgtcacgccccctcagccccccgctgagtcccttctctgttgtcgcgtcccgaatc
gagttccccggaatcagacggtgccccatagATGGCCAGCTTTCCCCCGAGGGTTAACG
AGAAAGAGATCGTGAGATCACCGTACTATAGGGGAACTCTTGGCTCCCAGCAGCTCCTTT
TGACAAGAAATGTGGTGGTGAGAACTGGACGGTTGCTTTTTGCTCcCTGATGGTTCCTAC
TTTGCGTGGTCACACAAGGATATCGCATAGTGAAGCTTGTCCCGTGGTCCCAGTGCCGTA
AGAACTTTCTTTTTGCATGGTTCCAAAAAATGTTACCAATTCAAGCTGTCTAAAATTGGC
AAGACAAAACAGTAATGGTGGTCAGAAAAACAAGCCTCCTGAGCACGTTATAGACTGT
GGAGACATAGTCTGGAGTCTTGCTTTTGGGTCTTCAGTTCCAGAAAAACAGAGTCGTT
GCGTTTAATATAGAATGGCATCGGTTCCGATTTGGACAGGATCAGCTACTCCTTGCCAC
AGGATTAAACAATGGTCGCATCAAAATCTGGGATGTATATACAGGAAAACTCCTCCTT
AATTTGGGTAGACCACATTGAAATGGTTAGAGATTTTAACTTTTGCTCCAGATGGGAGCT
TACTCCTTGTATCAGCTTCAAGAGACAAAAACTCTAAGAGTGTGGGACCTGAAAGATGA
TGGAAACATGGGTGAAAGTATTGCGGGCACATCAGAATTGGGtGtACAGTTGTGCATTc
TCTCCcGACTGTTcTATGCTGTGTTCAGTgGGCGCCAGTAAAGCAGTTTTcCTTTGGA
ATATGGATAAAtACACCATGATTAGGAAGctGGAAGGTCATCACCATGATGTTGTAGC

FIG 15(1)

TTGTGACTTTTCTCCTGATGGAGCATTGCTAgCTACTGCATCCTATGACACTCGTGTG

TATGTCTGGGATCCACACAATGGAGACCTTTCTGATGGAGTTTGGGCACCTGTTTCCCT

CGCCCACTCCAATATTTGCTGGAGGAGCAAATGACCGATGGGTGAGAGCTGTGTCTTT

CAGTCATGATGGACTGCATGTTGCCAGCCTTGCTGATGATAAAATGGTGAgGTTCTGG

AGAATCGATGAGGATTGTCCGGTACAAGTTGCACCTTTGAGCAATGGTCTTTGCTGTG

CCTTTTCTACTGATGGCAGTGTTTTTAGCTGCTGGGACACATGATGGAAGTGTGTATTT

TTGGGCCACTCCAAGGCAAGTCCCTAgCCTTCAACATATATGTCGCATGTCAATCCGA

AGAGTGATGTCCACCCAAGAAGTCCAAAAACTGCCTGTTCCTTCCAAAATATTGGCGT

TTCTCTCCTACCGCGCGGTTAGactgaagactgccttttcctggtaggcctgccagacaga

gcgcccttttacaagacacacctcaagctttacctcgtgccgaatt

FIG 15(II)

MASFPPRVNEKEIVRSRTIGELLAPAAPFDKKCGGENWTVAFAPDGSYFAWSQGYRIV

KLVPWSQCRKNFLLHGSKNVTNSSCLKLARQNSNGGQKNKPPEHVIDCGDIVWSLAFG

SSVPEKQSRCVNIEWHRFRFGQDQLLLLATGLNNGRIKIWDVYTGKLLLNLVDHIEMVR

DLTFAPDGSLLLVSASRDKTLRVWDLKDDGNMVKVLRAHQNWVYSCAFSPDCSMLCSV

GASKAVFLWNMDKYTMIRKLEGHHHDVVACDFSPDGALLATASYDTRVYVWDPHNGDL

LMEFGHLFPSPTPIFAGGANDRWVRAVSFSHDGLHVASLADDKMVRFWRIDEDCPVQV

APLSNGLCCAFSTDGSVLAAGTHDGSVYFWATPRQVPSLQHICEMSIRRVMSTQEVQK

LPVPSKILAFLSYRG*

FIG 16

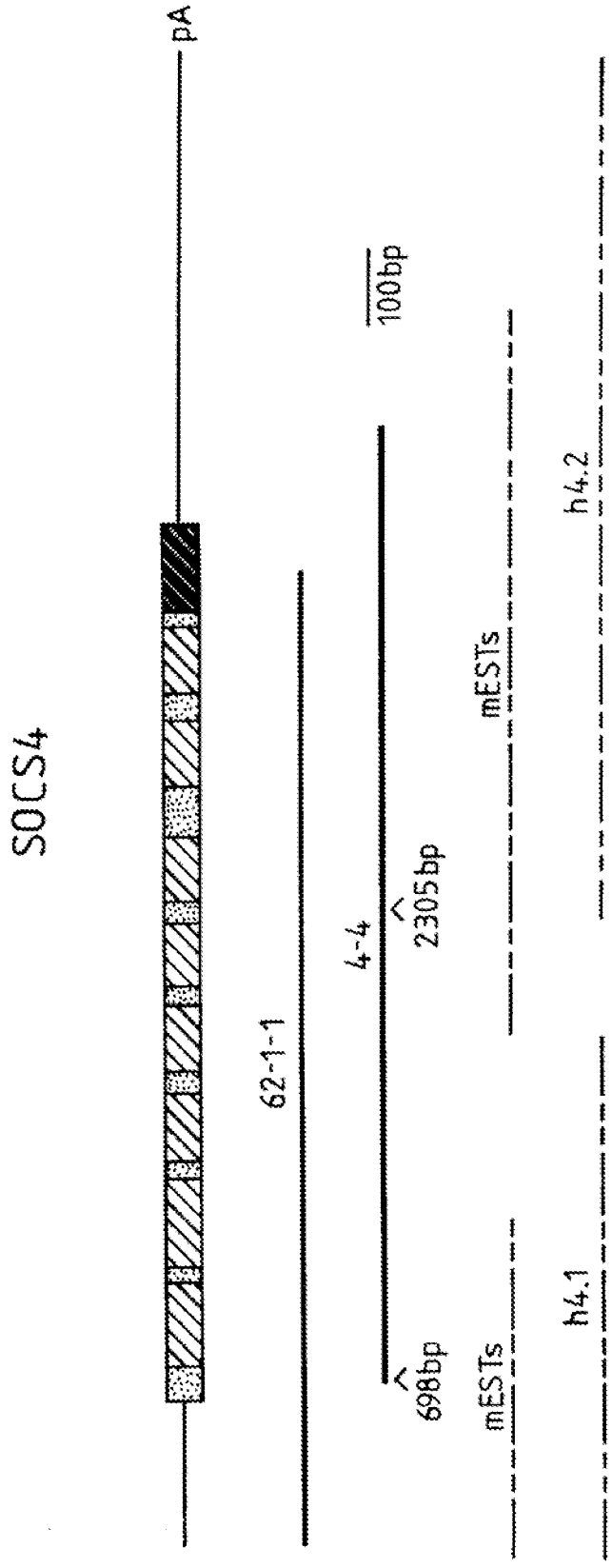


FIG 17

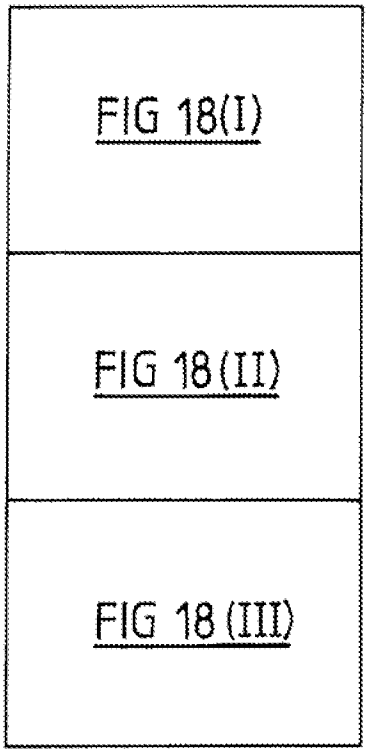


FIG 18

h4.1

CTGTCTTCCTCCGCAGCGCGAGGCTGGGTACAGGGTCTATTGTCTGTGGTTGACTCCG

TACTTTGGTCTGAGGCCTTCGGGAGCTTTCCCGAGGCAGTTAGCAGAAGCCGCAGCGA

CCGCCCCCGCCCGTCTCCCTCTGTCCCTGGGCCCGGGAGACAAACTTGGCGTCACGCCC

TCAGCGGTCGCCACTCTCTTCTCTGTTGTTGGGTCCGCATCGTATTCCCGGAATCAGA

CGGTGCCCCCATAGATGGCCAGCTTTCCCCCGAGGGTCAACGAGAAAGAGATCGTGAGA

TCACGTACTATAGGTGAACTTTTTAGCTCCTGCAGCTCCTTTTTGACAAGAAATGTGGTC

GTGAAAATTGGACTGTTGCTTTTTGCTCCAGATGGTTCATACTTTGCTTGGTCACAAGG

ACATCGCACAGTAAAGCTTGTTCCGTGGTCCCAGTGCCTTCAGAACTTTCTCTTGCAT

GGCACCAAGAATGTTACCAATTCAAGCAGTTTAAGATTGCCAAGACAAAATAGTGATG

GTGGTCAGAAAAATAAGCCTCGTGACATATTATAGACTGTGGAGATATAGTCTGGAGT

CTTGCTTTTTGGGTCATCAGTTCCAGAAAAACAGAGTCGCTGTGTAAATATAGAATGGC

ATCGCTTCAGATTTGGACAAGATCAGCTACTTCTTGCTACAGGGTTGAACAATGGGCG

TATCAAAATATGGGATGTATATTMCAGGAAACTCCCTCCTTAACTTGGTAGATCATACTG

AAGTGGTCAGAGATTTAACTTTTGCTCCAG

FIG 18(I)

h4.2

CTCTGTATGTCTGAATGAAGCTATAACATTTGCCTTTTTATTGCAGGTTTTCCTTTGG

AATATGGATAAATACACCATGATACGGAAACTAGAAGGACATCACCATGATGTGGTAG

CTTGTGACTTTTTCTCCTGATGGAGCATTACTGGCTACTGCATCTTATGATACTCGAGT

ATATATCTGGGATCCACATAATGGAGACATTCTGATGGAATTTGGGCACCTGTTTCCC

CCACCTACTCCAATATTTGCTGGAGGAGCAAATGACCGGTGGGTACGATCTGTATCTT

TTAGCCATGATGGACTGCATGTTGCAAGCCTTGCTGATGATAAAATGGTGAGGTTCTG

GAGAATTGATGAGGATTATCCAGTGCAAGTTGCACCTTTGAGCAATGGTCTTTGCTGT

GCCTTCTCTACTGATGGCAGTGTTTTAGCTGCTGGGACACATGACGGAAGTGTGTATT

TTTGGGCCACTCCACGGCAGGTCCCTAGCCTGCAACATTTATGTCGCATGTCAATCCG

AAGAGTGATGCCCACCCAAGAAGTTCAGGAGCTGCCGATTCCTTCCAAGCTTTTGGAG

TTTCTCTCCGTATCGTATTTAGAAGATTCTGCCTTCCCTAGTAGTAGGGACTGACAGAA

TACACTTAACACAAACCTCAAGCTTTACTGACTTCAATTATCTGTTTTTTAAAGACGTA

GAAGATTTATTTAATTTGATATGTTCTTGTACTGCATTTTGATCAGTTGAGCTTTTTAA

AATATTATTTATAGACAATAGAAGTATTTCTGAACATATCAAATATAAATTTTTTTTAA

AGATCTAACTGTGAAAACATACCTGTACATATTATTTAGATAAGCTGCTATATATGT

TGAATGGACCCTTTTGCTTTTCTGATTTTTTAGTTCTGACATGTATATATTGCTTCAGT

AGAGCCACAATATGTATCTTTGCTGTAAAGTGCAAGGAAATTTTTAAATTTCTGGGACAC

FIG 18(II)

TGAGTTAGATGGTAAATACTGACTTACGAAAGTTGAATTGGGTGAGGCGGGCAAATCA

CCTGAGGGTCAGCAGTTTGAGACTAGCCTGGCAAACATGATGAAACCCTGTCTCTACTA

AAAATACAAAAAAAAAAAAAA

FIG 18(III)

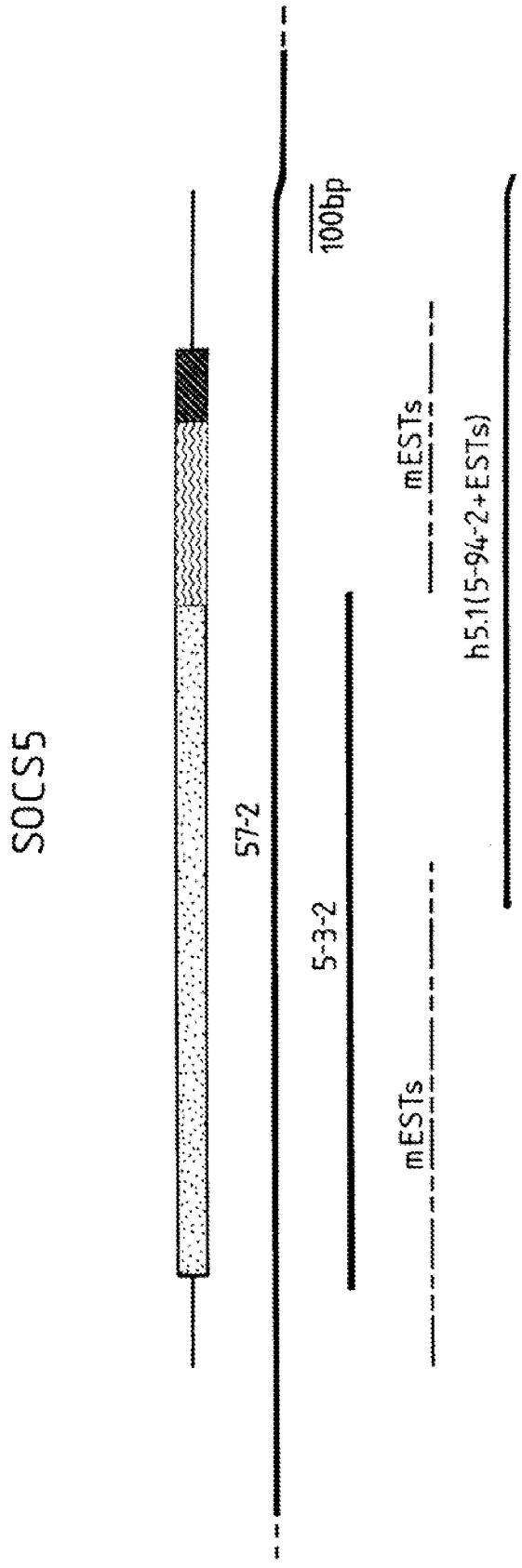


FIG 19

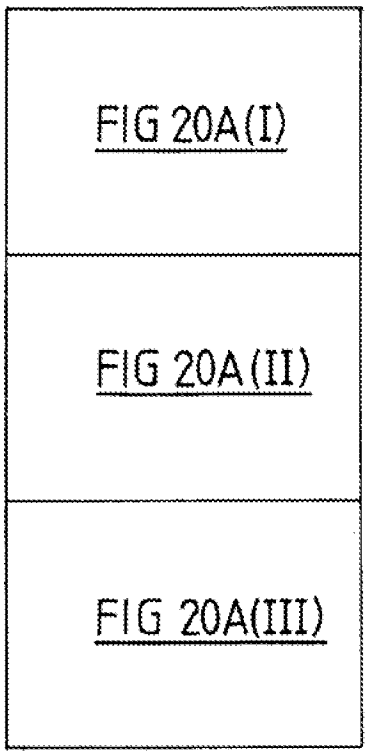


FIG 20A

cggcacgagccgggctccgtccggaggaagcgaggctgcgccggcccggcaggagc

ggaggacgggamgcgcgggcggtcgcgctcgccctgtcgctgactgcgctgccccggcc

catccttgccctggccgcaggtgccctggatgaggccgccgcgcgtgtcccggccgctga

gtgtccccccgcgggtcgccccggcgccgcctgccctcaagcggccgcctctcctgcccgggtc

cccgttttccccccggcgcgcagtccctcccggtgggcgccgcctcccgcacctcgggcgcaggcg

gcacggccctcgggccgggatccgccgcgggaagaggaagacaagccgggggcgttga

gcccctgcgcgcacgggtgccgccgcgcgtagtgggagcttactcgcagtaggctcctcgctc

ttctaaatcaATGGATAAAGTGGGGGAAAATGTGGAACAACTTAAAATACAGATGCCAGAA

TCTCTTCAGCCACGAGGGAGGAAGCCGTAATGAGAACGTGGAGATGAACCCCAACAGAT

GTCCGTCTGTCAAAGAGAAAAGCATCAGTCTGGGAGAGGCAGCTCCCCAGCAAGAGAG

CAGTCCCTTAAGAGAAAATGTTGCCTTACAGCTGGGACTGAGCCCTTCCAAGACCTTT

TCCAGGCGGAACCAAAACTGTGCCGCAGATCCCTCAAGTGGTTGAAATCAGCATCG

AGAAAGACAGTGACTCgGGTGCCCACCCCAGGAACGAGGCTTGCACGGAGAGACTCCTA

CTCGCGGCACGcCCCGTGGGGAGGAAAGAAGAAACATTCCTGTTCCACAAAGACCCAG

AGTTCATTGGATACCGAGAAAAAAGTTTGGTAGAACTCGAAGCGGCCTTCAGAGGCGAG

AGCGGCGCTATGGAGTCAGCTCCATGCAGGACATGGACAGCGTTTCTAGCCGCGCGGT

CGGGAGCCGCTCCCTGAGGCAGAGGCTCCAGGACACGGTGGGTTTGTGTTTCCCATG

AGAACTTACAGCAAGCAGTCAAAAGCCACTCTTTTCCAATAAAAGAAAAATACATCTTT

FIG 20A(I)

CTGAATTAATGCTGGAGAAATGCCCCTTTTCCTGCTGGCTCGGATTTAGCACAAAAGTG

GCATTTGATTAAACAGCATACCGCCCCCTGTGAGCCCCACACTCAACATTTTTTTGATACA

TTTGATCCATCACTGGTGTCTACAGAAGAAGATGAAGATAGGCTTCGCGAGAGAAGAC

GGCTTAGTATCGAAGAAGGGGTGGATTcCcCcTCCCAACGCACAAATACACACACCTTTGA

AGCTACTGCACAGGTCAACCCATTGTATAAGCTGGGACCAAAGTTAGCTCCTGGGATG

ACAGAGATAAGTGGAGATGGTTCTGCAATTCCACAAGCsAATTGTGACTCAGAAGAGG

ATTCAACCACCCCTATGTCTGCAGTCACGGAGGCAGAAGCAGCGCCAGGTGTCCGGGGA

CAGCCACGCGGCACGTTAGCAGACAGGGAGCTTGGAAAGTTCATACGCAGATCGATTAC

ATACACTGCCTCGTGCCAGATTTGCTTCAGATCACAGGGAATCCCTGTTACTGGGGCG

TGATGGACCGATACGAGGCCGAAGCCCTTCTAGAAGGGAAACCGGAAGGCACGTTCTT

GCTCAGGGACTCTGCACAGGAGGACTACCTCTTCTCTGTGAGcTTCCGCCGCTACAAC

AGGTCTCTGCACGCCCGGATCGAGCAGTGGAACCACACAACTTCAGCTTCGATGCCCATG

ACCCCTGCGTGTTCACTCCTCCACwGTCACGGGGCTTCTCGAACACACTATAAAGACCC

CAGCTCTTGCATGTTTTTTTGAACCGTTGCTAACGATATCACTGAATAGAACTTTCCCT

TTCAGCCTGCAGTATATCTGCCGCGCAGTGATCTGCAGATGCACTACGTATGATGGGA

TTGACGGGcTCCCGCTACCGTCGATGTTACAGGATTTTTTTAAAAGAGTATCATTATAA

ACAAAAAGTTAGGGTTCGCTGGTTAGAACGAGArCCAGTCAAAGCAAAGTAActcctg

tccccaaaggcactaactaagtctgctcctccccgtgcatcmgaactgcacccatagg

FIG 20A(II)

raggcagtcagctgctaggatttcccacccagaatgggagcttagtcattagcctctg

ccctatgggggtcccgctgttccctcagacaaaggtgccctagggacagcaagatggcttgc

aggtgttcgggtgggctgtgacaactgagggaggcaactctgggggcatttgctatgaag

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gactaaatgtttgaaattatttttctaagaatttttctataaccttcagaaaaaagtag

tgatgtttgtagttactataaaatcaagctttgaaaagttcaaaaacaaaacaagttaaata

aaagactacctttcctttttagagaaaaacaaatgcaagttttcccagcccacaggcattgt

gcactgttaatgttngcttgttatcagctccttttctcctcc

FIG 20A(III)

MDKVGKMWNNLKYRCQNLFSHEGGSRNENVEMNPNRCPSVKEKSISLGEAAPQQESSP

LRENVALQLGLSPSKTFSRRNQNCAAEIPQVVEISIEKDSDSCATPGTRLARRDSYSR

HAPWGGKKKHSCSTKTQSSLDTEKKFGRTRSGLQRRERRYGVSSMQDMDSVSSRAVGS

RSLRQRLQDTVGLCFPMRTYSKQSKPLFSNKRKIHLSELMLEKCPFPAGSDLAQKWHL

IKQHTAPVSPHSTFFDTFDPSLVSTEDEEDRLRERRRLSIEEGVDPPPNAQIHTFEAT

AQVNPLYKLGPKLAPGMTEISGDGSAIPQXNCDSEEDSTTLCLQSRRQKQRQVSGDSH

AHVSRQGAWKVHTQIDYIHCLVPDLLQITGNPCYWGVMDRYEAELLEGKPEGTFLLR

DSAQEDYLFSVSFRRYNRSLHARIEQWNHNFSFDAHDPCVFHSSXVTGLLEHYKDPSS

CMFFEPLLTISLNRTFPESLQYICRAVICRCTTYDGLDPLPSMLQDFLKEYHYKQK

VRVRWLERXPVKAK*

FIG 20B

GATTAAACAGCATACAGCTCCTGTGAGCCCACATTCAACATTTTTTGATACgTTTGATCCATCTTTGGTTT

CTACAGAAGATGAAGAAGATAGGCTTAGAGAGAAGGCGGCTTAGTATTGAAGAAGGGGTTGATCCC

CCTCCCAATGCACACAAATACATACATTTGAAGCTACTGCACAGGTTAATCCATTATwTAAACTGGGACCA

AAATTAGCTCCTGGAATGACTGAAATAAGTGGGGACAGTTCTGCAATTCCACAAGCTAATTGTGACTCG

GAAGAGGATACAACCACCCTGTGyTTGCAGTCACGGAGGCAGAAGCAGCGTCAGATATCTGGAGACAGC

CATACCCATGTTAGCAGACAGGGAGCTTGGAAAGTCCACACACAGATTGATTACATACACTGCTTCGTG

CCTGATTTGCTTCAAATTACAGGGAATCCCTGTTACTGGGGAGTGATGGACCGTTATGAAGCAGAAGCC

CTTCTCGAAGGGAAACCTGAAGGCACGTTTTTGCTCAGGGACTCTCTGCGCAAGAGGACTACTTCTTCTCT

GTGAGCTTCCGCCCGATACAACAGATCCCTGCATGCCCGAATTGAGGCAGTGGAATCACAACTTTAGTTTC

GACGCCCATGACCCGTGTGTATTTCACTCCTCCACTGTAACGGGACTTTTAGAACATTATAAAGATCCCA

GTTCGTGCATGTTTTTTGAACCATTGCTTACTATATCACTAAATAGGACTTTCCCTTTTAGCCTGCAGTAT

ATCTgTcGCGCCGGTAATCTGCAGGTGCACTACGTATGATTGAATTGATGGGCTCCCTCTACCCTCAATGT

TACAGGATTTTTTTAAAAGAGTATCATTATAAACAAAAAAGTTAGAGTTCGCTGGTTGGaACGAGAACCAG

TCAAGGCAAAGTAAACTCTCCGGTCCCCAAAGGgTGTTAACTAGGTCCGCTTTCATGTGCATCAGACAGT

ACACCTATAGCAAGCACACGTAGCAGTGTTAGGCTTTTTCATACAGTATGTAAGcTTAGTGTTATCT

GTCAGAtGCTACCTGCTGTTACTTATTCAGATAAAACATGGtGCCTATTGGAACAATAGcGGATAGAGCTAC

AGGTGTTCAGTAAGACTACAAAAAACATTTTGCCTATTTCGCTAACAGTTTGGTTTTTAATGGCTGTGGtA

TTTGAGTGAGGCAACTCTGGGGCATTTGTTATGAAGAAATG

FIG 21

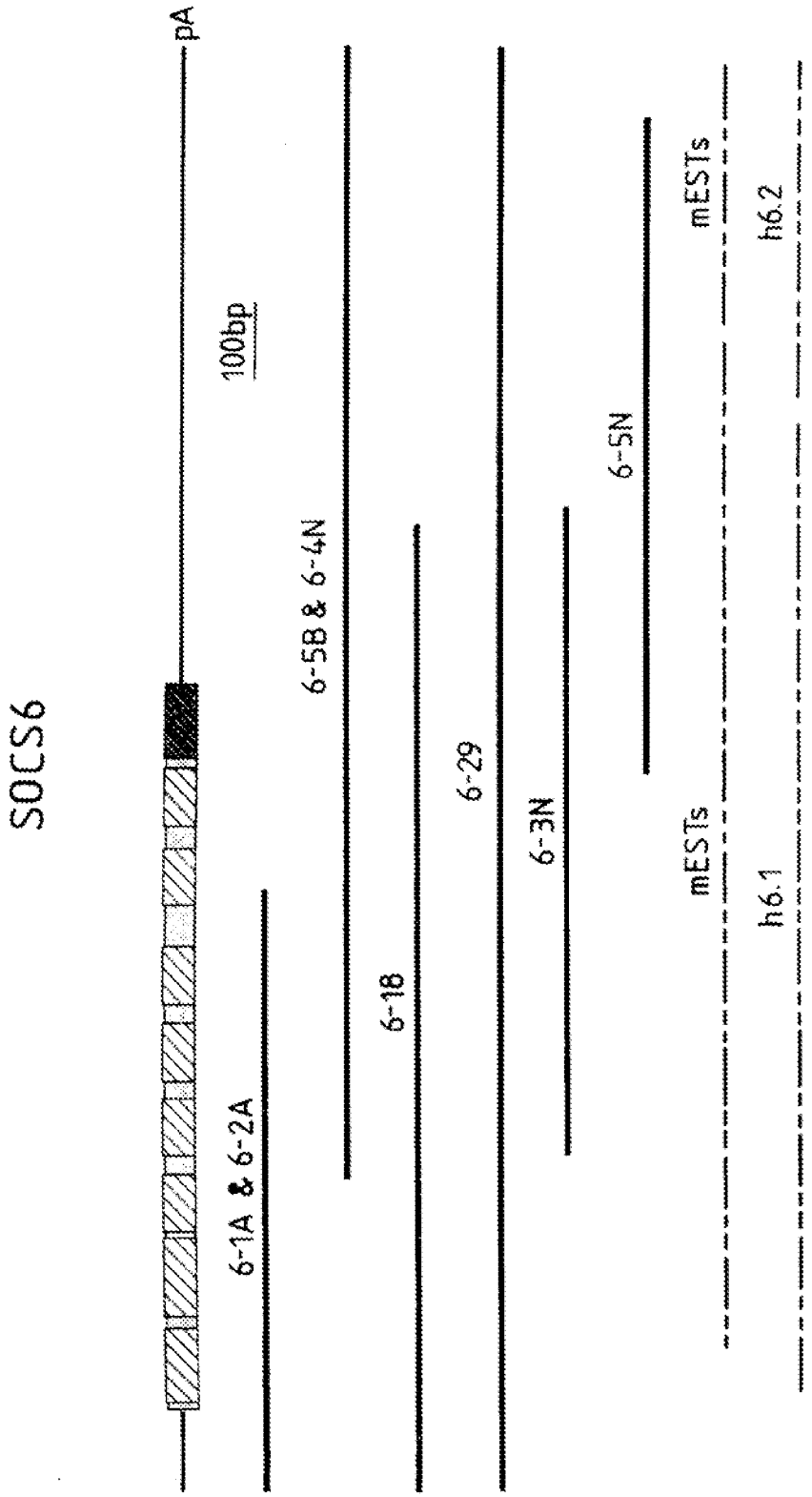

SOCS6
pA
100bp
6-1A & 6-2A
6-5B & 6-4N
6-18
6-29
6-3N
6-5N
mESTs
h6.1
mESTs
h6.2

FIG 22

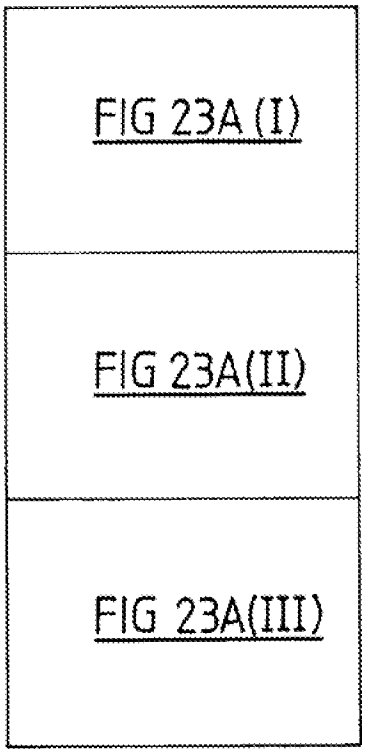


FIG 23A

```
ggcacgaggcggtggtggcggcggcgccgcggcgggcgggcgcggaATGA
AGGCCCACGGCCCTGGGGGCTGAGGCGCCCGCCTGGGGCGGCCGCGTCCTCA
TGGAGGCCGCGAGAGGAGCCGCTGCTGGCTGAACTCAAGCCTGGGCGCCCCCACCA
GTTCGACTGGAAGTCAAGCTGCGAGACCTGGAGGCGTGGCCTTCTCGCCAGACGGTTCC
TGGTTCGCCTGGTCTCAAGGACACTGCGTGGTCAAGCTGGTCCCCTGGCCCTTAGAGG
AACAGTTCATCCCTAAAGGATTCGAAGCCAAGAGGCCGAAGCAGCAAGAATGACCCAAA
AGGACGGGGCAGTCTGAAGGAGAAGACGCTGGACTGTGGCCAGATTGTGTGGGGGCTG
GCCTTCAGCCCGTGGCCCTCTCCACCCAGCAGGAAACTCTGGGCACGTCACCATCCCC
AGGCGCCTGATGTTTCTTGCCTGATCCTGGCCACAGGTCTCAACGATGGGCAGATCAA
GATTTGGGAGGTACAGACAGGCCTCCTGCTTCTGAATCTTTCTGGCCACCAAGACGTC
GTGAGAGATCTGAGCTTCACGCCCAGCGGCAGTTTGATTTTGGTCTCTGCATCCCGGG
ATAAGACACTTCGAATTTGGGACCTGAATAAaCACGGTAAGCAGATCCAGGTGTTATC
CGGCCATCTGCAGTGGGTTTACTGCTGCTCCATCTCCCCTGACTGTAGCATGCTGTGC
TCTGCAGCTGGGGAGAAGTCGGTCTTTCTGTGGAGCATGCGGTCCTACACACTAATCC
CGAAACTAGAAGGCCACCAAAGCAGTGTTGTCTCCTGTGATTTCTCTCCTGATTCAGC
CTTGCTTGTCACAGCTTCGTATGACACCAGTGTGATTATGTGGGACCCCcTACACCGGC
GcGAGGCTGAGGTCACTTCATCACACACAACTTGAACCCACCATGGATGACAGTGACG
TCCACATGAGCTCCCTGAGGTCCGTGTGCTTCTCACCTGAAGGCTTGTATCTCGCTAC
```

FIG 23A(I)

GGTGGCAGATGACAGGCTGCTCAGGATCTGGGCTCTGGAACTGAAGGCTCCGGTTGCC
TTTGCTCCGATGACCAATGGTCTTTGCTGCACGTTCTTCCCACACGGTGGAATTATTG
CCACAGGGACGAGAGATGGCCATGTCCAGTTCTGGACAGCTCCCCGGGTCCTGTCCTC
ACTGAAGCACTTATGCAGGAAAGCCCTCCGAAGTTTCCTGACAACGTATCAAGTCCTA
GCACTGCCCAATCCCCCAAGAAGATGAAAGAGTTCCTCACATACAGGACTTTCTAGcagt
gccggctccccacctcctgcagcagcagtacaaagggactggctaggatggagtc
aggcagctcacactggaccagtgtggacctttcctcccatggcatgtgcaagtag
gtctgcgtgtgacccccacttcctgtgggtgccggccttacctcgtcttcatccgtggtgtgagc
agccttcgtcagtctagttgtgttgaagccaagtgcagtttgtggatggttgctgggggta
ataaaggcaagcgggctcccagagcctcttctggtggcggccaaggccacactccccttaac
tgggaagtacctgccacgtagggcatttctgctgcctatttccagccggctgcat
ggtttgaagttccctccgttgttgtggtcagaagaactcctggtgttttggttccctgctcagc
tgcgcgtggactgggctgaggctccctcaccatacactagtgccggctttttgtttcctgt
aaacagtgggttgcatgtgtagagaggaagtaacaagcgagtattcagatcatacgaggagg
cgttccctcggtgcatgacgggtcagatggccatttatcatcagcatatttattttgtatttttc
tcagcacatagtaaggtacaactgtgtttttctcaattgtctcgaaaaaacagagttct
taagtggcccagtttgtggagccaagtctaagtcgtgtggagtcagtgctgacatcact
ggcttgtgctgtctgtcacatgtgtttgtctctgctgcttgacctcatgggatgtacc

FIG 23A(II)

ctccagttcaactgcccaaaaacagacagccccttccaagcaccgttctttgacagcgg
tagcagctacctattcaagacgcctcacacaaaatctgccttagaaagttaatatatt
ttaaattatttttaaaagaaactcaacatcttatttctttggccttttcttaattgatgct
ttatggaggcagtgttaacattgtacagtgtatgcatagaggagtcctcctctatttga
agaacaatgcaaaatgaggctttcattgaagggaaaaaaaaaaaaaaa

FIG 23A(III)

MEAGEEPLLLAELKPGRPHQFDWKSSCETWSVAFSPDGSWFAWSQGHCVVKLVPWPLE

EQFIPKGFEAKSRSSKNDPKGRGSLKEKTLDCGQIVWGLAFSPWPSPPSRKLWARHHP

QAPDVSCLILATGLNDGQIKIWEVQTGLLLLNLSGHQDVVRDLSFTPSGSLILVSASR

DKTLRIWDLNKHGKQIQVLSGHLQWVYCCSISPDCSMLCSAAGEKSVFLWSMRSYTLI

RKLEGHQSSVVSCDFSPDSALLVTASYDTSVIMWDPYTGARLRSLHHTQLEPTMDDSD

VHMSSLRSVCFSPEGLYLATVADDRLLRIWALELKAPVAFAPMTNGLCCTFFPHGGII

ATGTRDGHVQFWTAPRVLSSLKHLCRKALRSFLTTYQVLALPIPKKMKEELTYRTF*

FIG 23B

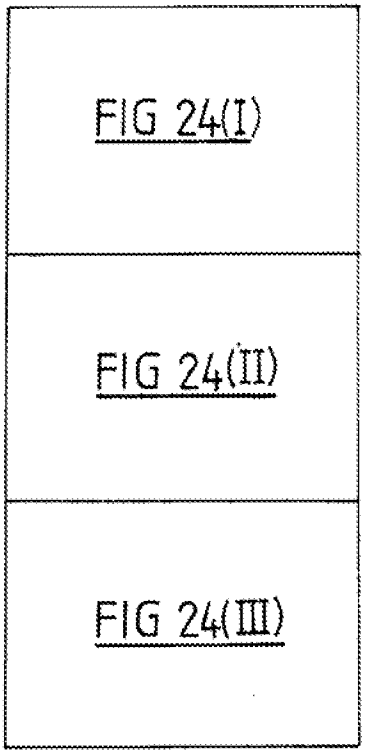


FIG 24

h6.1

GACACTGCATCGTCAAACTGATCCCCTGGCCGTTGGAGGAGCAGTTCATCCCTAAAGG

GTTTGAAGCCAAAAGCCGAAGTAGCAAAAATGAGACGAAAGGGCGGGGCAGCCCAAAA

GAGAAGACGCTGGACTGTGGTCAGATTGTCTGGGGGGCTGGCCTTCAGCCTGTGNCTTT

CCCCACCCAGCAGGAAGCTCTGGGCACGCCACCCCCAAGTGCCCGATGTCTCTTG

CCTGGTTCTTGCTACGGGACTCAACGATCAAGATCTGGGAGGTGCAGACA

GGGCTCCTGCTTTTGAATCTTTCCGGCCACCAAGATGTCGTGAGAGATCTGAGCTTCA

CACCCAGTGGCAGTTTGATTTTGGTCTCCGCGTCACGGGATAAGACTCTTCGCATCTG

GGACCTGAATAAACACGGTAAACAGATTCAAGTGTTATCGGGCCACCTGCAGTGGGTT

TACTGCTGTTCCATCTCCCCAGACTGCAGCATGCTGTGCTCTGCAGCTGGAGAGAAGT

CGGTCTTTCTATGGAGCATGAGGTCCTACACGTTAATTCGGAAGCTAGAGGGCCATCA

AAGCAGTGTTGTCTCTTGTGACTTTCTCCCCCCGACTCTCTGCCCTGTTGTCACGGCTTCT

TACGATACCAATGTGATTATGTGGGACCCCCTACACCGGCGAAAGGCTGAGGTCACTCC

ACCACACCCAGGTTGACCCCCGCCATGGATGACAGTGACGTCCACATTAGCTCACTGAG

ATCTGTGTGCTTCTCTCCAGAAGGCTTGTACCTTGCCACGGTGGCAGATGACAGACTC

CTCAGGATCTGGGCCCTGGAACTGAAAACTCCCATTGCATTTGCTCCTATGACCAATG

GGCTTTGCCTGGCACATTTTTTCCACATGGTGGAGTCATTGCCACAGGGACAAGAGATG

GCCACGTCCAGTTCTGGACAGCTCCTAGGGTCCTGTCCTCACTGAAGCACTTATGCCG

FIG 24(I)

GAAAGCCCTTCGAAGTTTCCTAACAACTTACCAAGTCCTAGCACTGCCAATCCCCCAAG

AAAATGAAAGAGTTCCTCACATACAGGACTTTTTTAAGCAACACCACATCTTGTGCTTC

TTTGTAGCAGGGTAAATCGTCCTGTCAAAGGGAGTTGCTGGAATAATGGGCCAAACAT

CTGGTCTTGCATTGAAATAGCATTTCTTTGGGATTGTGAATAGAATGTAGCAAAACCA

GATTCCAGTGTACTAGTCATGGATTTTTC

FIG 24(II)

h6.2

ACCATGGTTCCAAGWTCCTCTCCYKCCTGTGGTCMRAAGTTGCYYCCGAATGTTGGGC

CCAAGTGCCTTTTCYCTCCTTGGGCCTCCCCTTCTGACCTGCAGGACAGTTTTCCYGG

AGCCCATTTGGTATGAGGTATTAAWTTAGCCTTAACTAAATTACAGGGGACTCAGAGG

CCGTGCTCCTGACCGATCCAGACACTATTTTTTTTTTTTTTTTTAACAATGGTGTGC

ATGTGCAGGAAATGACAAATTTGTATGTCAGATTATACAAGGATGTATTCTTAAACCG

CATGACTATTCAGATGGCTACTGAGTTATCAGTGGCCATTTATTAGCATCATATTTAT

TTGTATTTTTCTCAACAGATGTTAAGGTACAACTGTGTTTTTTCTCGATTATCTAAAAAC

CATAGTACTTAAATTGAAAAAAAAAA

FIG 24(III)

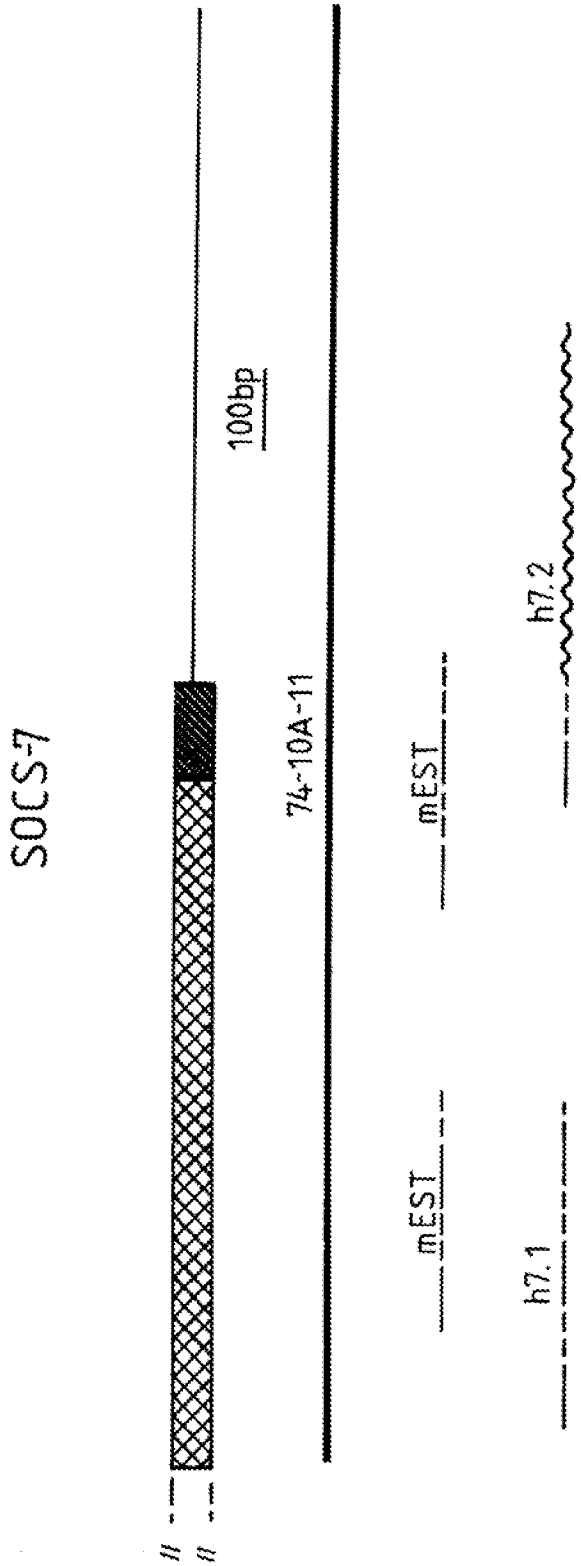


FIG 25

FIG 26A(I)

FIG 26A(II)

FIG 26A

GGCACCAGAGGCCGGGGTCAGGGCCGGAGGCTGAGGACCAAGTAGGCATGGCGGAGGGCGGG

ACCGGCCCCCCGATGGACGGGGCCCGGCCCCGCAGGTCCTCCTAATCTGAAGGAGTGGC

TGAGGGAGCAGTTCTGTGACCATCCACTGGAGCACTGTGACGATACAAGACTCCATGA

TGCAGCCTATGTAGGGGACCTCCAGACCCCTCAGGAACCTACTGCAAGAGGAGAGCTAC

CGGAGCCGCATCAATGAGAAGTCTGTCTGGTGCTGCGGCTGGCTTCCCTGCACACCAC

TGAGGATCGCAGCCACTGCAGGCCATGGGAACTGTGTGGACTTCCTCATACGCAAAGG

GGCCGAGGTGGACCTGGTGGATGTCAAGGGGCAGACTGCCCCTGTATGTGGCTGTAGTG

AACGGGCACTTGGAGAGCACTGAGATCCTTTTTGGAAGCTGGTGCTGATCCCAACGGCA

GCCGGCACCACCGCAGCACTCCTGTGTACCATGCCTyTCGTGTGGGTAGGGACGACAT

CCTGAAGGCTCTTATCAGGTATGGGGCAGATGTTGATGTCAACCATCATCTGAATTCT

GACACCCGGCCCCCTTTTTCACGGGCGGCTAACCTCCTTGGTGGTCTGTCCTCTATACA

TCAGTGCTGCCTACCATAACCTTCAGTGCTTCAGGCTGCTCTTGCAGGCTGGGGCAAA

TCCTGACTTCAATTGCAATGGCCCTGTCAACACCCAGGAGTTCTACAGGGGATCCCCT

GGGTGTGTCATGGATGCTGTCCTGCGCCATGGCTGTGAAGCAGCCTTCGTGAGTCTGT

TGGTAGAGTTTGGAGCCAACCTGAACCTGGTGAAGTGGGAATCCCTGGGCCCAGAGGC

AAGAGGCAGAAGAAGATGGATCCTGAGGCCTTGCAGGTCTTTAAAGAGGCCAGAAGT

ATTCCCAGGACCTTGCTGAGTTTGTGCCGGGTGGCTGTGAGAAGAGCTCTTGGCAAAT

ACCGACTGCATCTGGTTCCCTCGCTGCCAGACCCCATAAAGAAGTTTTTGCT

FIG 26A(I)

TTATGAGTAGCattcacatgcagtgctgactgcaatgtggaagccgatcacctgcagt
gaaaactgacacagactctggcatcctgggaaccatggcctgtgctgccagcttgatc
cttggctgtcagtgaagaaaaacggctgttctcttggactgtgattctatctcag
gtgcttgggccatcgaacgctccttgagtcattgtcaactgagaggcacatacaaact
taatttttgttccctcttcagtctcttctgtttttggattcttccctggcaatgtgtgcagca
tgggctgagccctggtgattgccctagtgggggaaggctttttttcccaggctatgcatc
tatttatgttccctactttgcaatttattattgttctttttaaggcttgatatcaaaaacagaa
agaggtttgttaagaaaaagatatagggagaaaaggaattccggttccgtgcacttgcta
gcctgctttccttgccctgggtttgtctgtctatgctgccctggtgcacatccctttctct
ttgctgccactgttctatttttgggagtttgtctttccgtctaagatggcttctgggggttc
tatcttattgcacagagggtcccagaacagtgttcatagggcaccatctgctctgccaa
gggttttctgatgtctttaccctgggggatcttcagacagtggttacctttaggagaccc
acctggaactaaccattaagtgactgcccacattcagatcagggaccatcttaatagt
actcactgccagtccctcacaagagaagatgacacgggtgctctcttcagacactccca
tacaggaagttgggaaaatgtcttgggtcacctgggttgttccccaggctacaacttcttg
gtgttccactaaraccagratatccctagttttttgggttgactgttccctccccactt
tccttgaancccaatgcccnttttgtktnggttgctttccctaaaaktt

FIG 26A(II)

.....ARGGVRAEAEDQVGMAEGGTGPDGRAGPGPAGPNLKEWLREQFCDHPLEHCDDT

RLHDAAYVGDLQTLRNLLQEESYRSRINEKSVWCCGWLPCTPLRIAATAGHGNCVDFL

IRKGAEVDLVDVKGQTALYVAVVNGHLESTEILLEAGADPNGSRHHRSTPVYHAXRVG

RDDILKALIRYGADVDVNHHLNSDTRPPFSRRLTSLVVCPLYISAAYHNLQCFRLLLQ

AGANPDFNCNGPVNTQEFYRGSPGCVMDAVLRHGCEAAFVSLLVEFGANLNLVKWESL

GPEARGRRKMDPEALQVFKEARSIPRTLLSLCRVAVRRALGKYRLHLVPSLPLPDPIK

KFLLYE*

FIG 26B

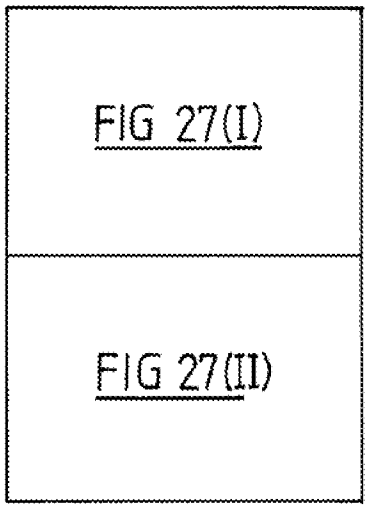


FIG 27

h7.1

GCATCCATGGCGGAGGGCGGCAGCACGACGGGCGGGCCAGGGCCGGGCTCCGCAGGTCG

TAATCTGAAGGAGTGGCTGAGGGAGCAATTTTGTGATCATCCGCTGGAGCACTGTGAG

GACACGAGGCTCCATGATGCAGCTTACGTCGGGGACCTCCAGACCCTCAGGAGCCTAT

TGCAAGAGGAGAGCTACCGGAGCCCGCATCAACGAGAAGTCTGTCTGGTGCTGTGGCTG

GCTCCCCTGCACACCGTTGCGAATCGCGGCCACTGCAGGCCATGTGTGGAGCTGTGGAC

TTCCTCATCCGGAAGGGGGCCGAGGTGGATCTGGTGGACGTAAAAGGACAGACGGCCC

TGTATGTGGCTGTGGTGAACGGGCACCTAGAGAGTACCCAGATCCTTCTTCTCGAAGCTGG

CGCGGACCCCCAAC

FIG 27(I)

h7.2

GAGGAAGAAGAAAAAGTGGACCCTGAGGCCTTGCAGGTCTTTAAAGAGGCCAGAAGTGT

TCCCAGAACCTTGCTGTGTCTGTGCCGTGTGGCTGTGAGAAGAGCTCTTGGCAAAMAC

CGGCTTCATCTGATTCCTTCGCTGCCTCTGCCAGACCCCATAAAGAAGTTTCTACTCC

ATGAGTAGACTCCAAGTGCTGCGGTTGATTCCAGTGAGGGAGAAAGTGATCTGCAGGG

AGGTGGACACCGAGCCCTGAGTGCTGTGCTGGCTGGTCTCCTGATGGCTGTTGCTG

CAGAAGATGTGTCCTCGTAGACTGTCATTGCTCCTCAGGTGCCTGGGCCGCTGAACAGTC

CTTGGGTCATTGTCAGCTGAGAGGCTTATACTAAAGTTATTATTGTTTTTTCCCAAGTT

CTCTGTTCTGGATTTTTCAGTTGCATATTAATGTAACGGGCCATGGGGTATGTACATGT

AGGGGCTGAGGTTGGAGGCCTACTAATTTCCTGTAGGGAAGACTCCCAGCACTTCTGG

AACTGTGCTTCTCTTTATTTTTCTACTTCTCAATTTGATGGTTCGATTAAAGCCTTCT

AGTATCTCAATGAAAA

FIG 27(II)

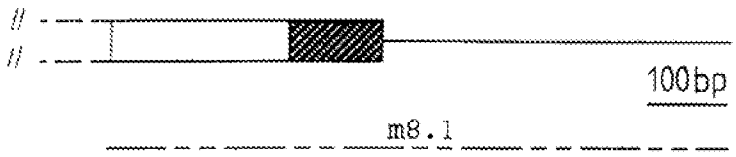


FIG 28

C'TGATGTCCGCAATTCTGAAGGTTGGACACCACTGCTGGCTGCCTGTGACATCCGCTG

TCAATCCCCCAAAGGATGCTGAGGCCACCCACCAACCGCTGTTTTCAACTGTGCCGCTTG

CTGCTGTCTGTGGGGGCAGATGCTGATGAATACATACCGTGTAGTTCAGCTTCCTGAG

GAGGCCAAGGgCTTGGTGCCACCAGAGATTCTACAGAAGTACCATGGATTCTACTCTT

CCCTCTTTGCCTTGGTGAGGCAGCCCAGGTCGCTGCAGCATCTCTGCCGTTGTGCGCT

CCGCAGTCACCTGGAGGGCTGTCTGCCCCATGCACTACCGCGCCTTCCCCTGCCACCG

CGCATGCCTCCCGCTTTCTGCAGCTGGACTTTTGAGGATCTGCTCTACTAGgctttgcctgcc

ctgtgaacaaagcagaccccaccccccaaggggcatcctctcagcaatgaatgatg

caaggcggtctgtcttcaagtcaggagtggacgccttgatccacacttgagagaagag

gccagatcagcaccyggctggtagtgatngcagagggcacctgtgcagatctgtgtgc

gcactggaaatctctaggctgaaggcyagagcaaatgggtgcargtgttagtccttgggg

angagagacagaganggtgagaaaagcaagacagaggtgagagtgcacatgtcaagtggta

gattgccttaaaagaaagctaaaaaaaaagaaaaagatttcgggcgaacttctttagggggt

aatgctgcagcgtgttaaaactgaccagcgtccatatctttggaccccttcccgggg

tgaaaaagccccttcatcctccagcgctcccccaagggtgcttagcaataccgggtgct

ttctctgccgcaaagtgagttaccaaa

FIG 29A

....MSAILKVGHHCWLPVTSAVNPQRMLRPPPTAVFNCAACCCLWGQMLMNTYRVVQ
LPEEAKGLVPPEILQKYHGFYSSLFALVRQPRSLQHLCRCALRSHLEGCLPHALPRLP
LPPRMLREFLQLDFEDLLY*

FIG 29B

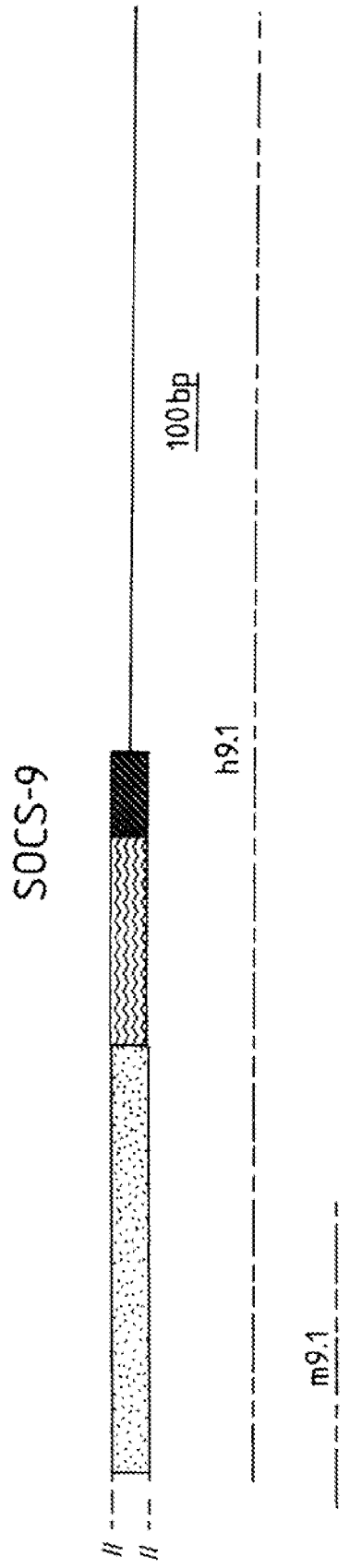


FIG 30

GTGGGGGCGTCATCATGACCTCCTCTAGGGCTCTGCAACATGACTCCTGTGGTGCAAA

TCAACAAATTGTTCACTGATGAATCCACACAAGGATCTCTGGGCCTACAACCAGGTCCTG

GTCCACATGACTGTCGTCTTCGGAGAAGGCACCACTCGCCCCCGGCAGGTACGGCTGA

CACCTCCATGGGAGAAGACGTATCCAGGCAGCTGCGCGGCCCTTCAAGAGGGCAC

ATCCCCGTCATCTAAAGGCACGGTGTACTGAAGCGTAGTCCTGAGACATGAGTCCGATTA

CTACAGGCACGTGTTCCTCCAGGTGGAGGCTCAGGTCCCCGGGTGAGCTGGGGCTGCA

GCGGGACTCAGGGCGCGGCTCTGGCTGCAGGTCTCGCAGCTCCCTGGGCTGTAGCTCC

CGCAGATCCTTGCGCACACCGTTGACTGGT

FIG 31

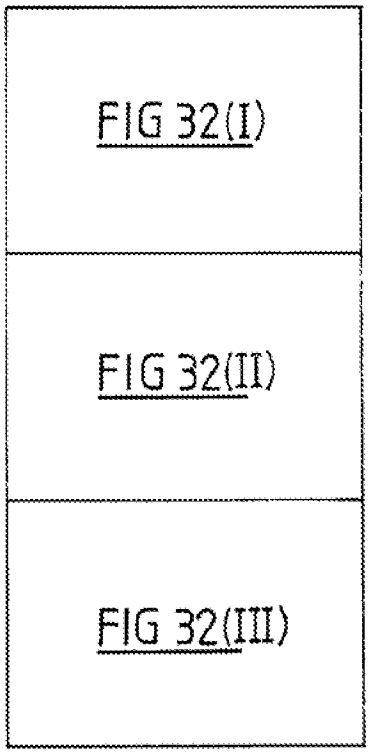


FIG 32

TTAATAGTACCTACATAGTAGAAAATTATAACTCCACTTTAAAACAATGTTTTTCTTTC

TATTCAAATCAATTTTAAAACTTTTTATAAACATTAATGTTGCAAGAGAATCCAGTCCA

TTTATGAAAATTAGTTGACAATCAAGTTCACCCAAGAAAATGTTGACTAAGCTAAAGA

AATCACAGATAAAACATTTTACCAAAAGGATAGGTAACACACAAAAAATGCTATCAC

AGGAAGCTNATGATCATCTAATATTTCTTTAATAATTCTAGTTCCATAGGTTTTTC

ATGTTTATGCCAATTTGTACCCGAGTTTAATTACAGAAAGGCAACAATTTCTAAATTG

GTGGTATACATTTCTTTACAATTTTTTTAATGTAAGGCCATTTATTAAAATAGACAAAC

TAGAAGATGAAAACGAAGGCAACAGAAAAATTCAACTTTTCACAACCAAAAGAATTAG

CACAACCTTAGAAATAATTTAGAAAAAAGTGTTGTTAAAAGATATGTTGCAGATCTCC

GTTCCATTACCCAAGATTATGTCAATTCACGATTCTAAATAAATCTTTTTTAAACGTAAG

AGATTAAAAACTCATCTTCAGTGTATATGTAAATTCCGTGGTTTTTATCACACAGGTAT

GTTTATTCAACACACTGKCTTTGGAAANTGGACCATTTAAAAGGACATGGCAATTTCCAT

TCTGTTAAGTTTCATTCAACCTTTACTTAGGGGTTGRATTACCACATGAAATGNTGCT

TTTAATGCATAAAAATCACAGTGGATTAGCCAGCAAAAGGGACTGGGCGGGGGGGCA

TTGAGGAGAATTTTGATAATTCACATTGTGATTATTCTGCACATTGATGAACATAATT

CACACCTCTAAAACCTCAAGACTTCCCTTTTTTAAAGAACCCAAAATAAACCCAAGACA

CCTTGCTGACACTTCCCCACCCCTAAACAAACTGATGACTCTTTTTACACATAAAACTG

AAATAGTTATGGCAGCAAAAGATTTTTGATGGCAATGAAAGTTTGTAAACTGTATTTCA

FIG 32(I)

ATCTCTTGTTCTTATTCCCAAAGTGCAAGATGCAGGGTTCTCAATCTTTCAGTAGTGC
TTCTCCTGTAAATAATCCTTCATTTTGTTTGGCAAAGGCAGTTTCTGAATTAAGTCTA
TTCTGGTATACTGACGTATAACAAAACGACACAGGTACTGCAACGAGCGCACCTSSAT
GAACNCCCGRGAACACTGGSTTGGYCAAGTTCTNGACRRGGKAAGKTGCAGATTCCAG
GCAGCYGAGACCTTGAATAACAAAAAGCTCCCATTTTCAGAGTCCCTGATTGAATGCT
CCAATTAGATCAACTATGGACGTATGTCCTTCCACATCNGGCTGTTCATAAAAGCTAA
ACCTACCATTTGAGTGCTCAATTCTAGTGTGAAGTGTTTTACCATGGGAGCGAAAGTC
ACAGCTTAAAAGGTAACGGTCGTCAGAACTGTCCCGAACAAGAAAGAACCATCTGGC
ACGTTTGCTAGCTTCCCTCTGCCTCCCAACGTGTGATTGGTCCCCAGTACCATCCTT
GCTTTGCAAGTTTTTTTCAGCTCCTCTGTAAGGCTTGTCACAACCATGGGACCACTACT
TTGCACTGAGTCATAAACTCTTGCAACCCCAGGAGCAGAGTTCGGATCAAAATTCAAA
TGACAGCGCATAACTTTTNCAGCCACGTGGGGCTTTCTGTSCCAGTGAGTCCACTGAAA
GTTCCCCTTTTGGGATTTGGATTATTCCTGCATTGGAGNTAACCAATGGTGAAGATTGG
AGGGACATCCATCGTGAACCCGCTCTCCGGGGTTCTGCAACATGACTCCCGTGGTGCC
AATCAACAAGCCATTCACCGGACTGATCCACGAAGATCTCTGGGGCGACAACTAGGTC
CTGGTCTACCTGACTCTCATCCTCGGGGAAAGCGCGCCCTCCCACTTGAGGAGGAACC
GCAGAGACTTCCATGGGAGAAGAGCTGTCCAGACAATAGCTCCGTGATCCTTCCAAAG
GATACATCCCCTCATCTAAAGGCACAGTATACTGAATGTAGTCCTGAGGCATAAGTCC

FIG 32(II)

AATAACGACAGGCACATGTTCATCCAGGTGAAGATGCAGGTCTCCATTATGAGAAGCC

GAGCTTCTTCAGTGAATTGGCTTGCTCCTGGCACGTGGTCTCAGACTGGAGGTCGT

FIG 32(III)

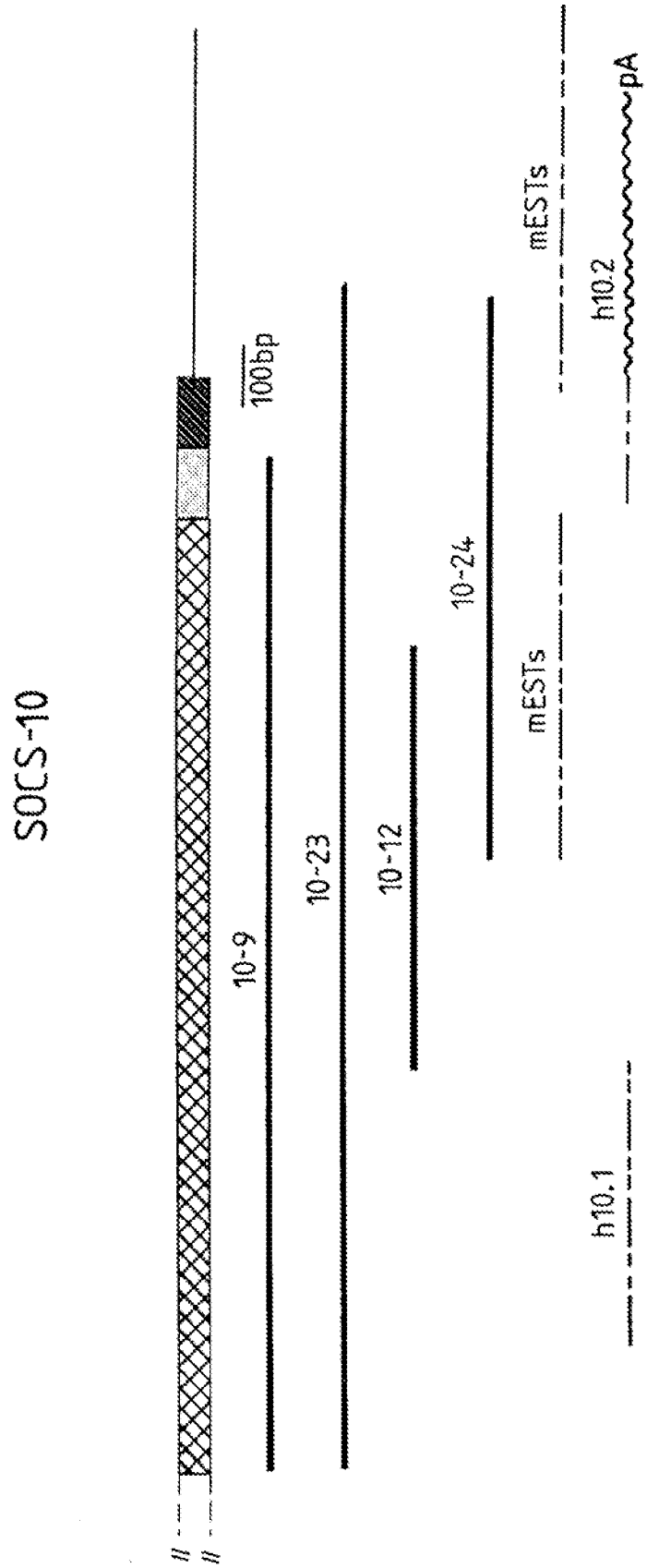


FIG 33

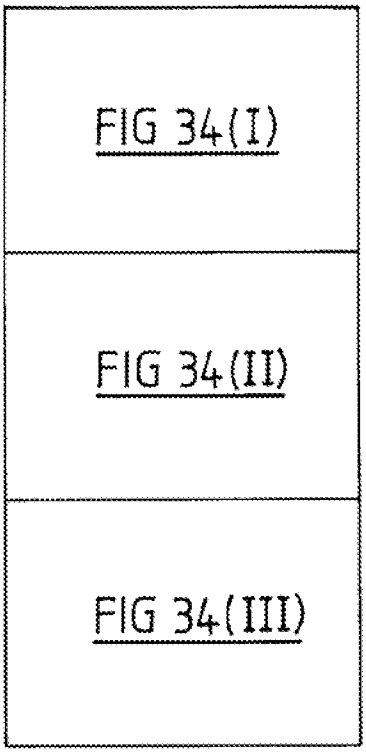


FIG 34

GGCACGAGGCTGTGTCCAGCACACAGAGAGGGCCCGGCCATCTGCTTTGGTTCAGAGC
CCTGTGTCTGTCTGTCACTTAGACTCTTCCTCCCGGCTCGCAGCTCACCCTCCATCCT
CCTTACTGGCTCCAGCATGACTCGCTTCTCTTATGCAGAGTACTTTGCTCTGTTTCAC
TCTGGCTCTGCACCTTCCAGGTCCCCTTCGTCTCCCGAGAACCCACCGGCCCGCGCAC
CCCTGGGTCTGTTCCAAGGGGTCATGCAGAAGTATAGCAGCAACCTGTTCAAGACCTC
CCAGATGGCGGCTATGGACCCCGTGCTGAAGGCCATCAAGGAAGGGGATGAAGAGGCC
TTGAAGATCATGATCCAGGATGGGAAGAATCTTTGCAGAGCCCAACAAGGAGGGCTGGC
TGCCGCTCCACGAGGCTGCCTACTATGGCCAGCTGGGCTGCCTGAAAGTCCTGCAGCA
AGCCTACCCAGGGACCATTGACCAACGCACACTGCAGGAAGAGACAGCATTATACCTG
GCCACATGCAGAGAACACCTGGATTGCCTCCTGTCGCTGCTCCAGGCGGGGGCAGAGC
CTGACATCTCTAACAAATCCAGGAGACTCCCACTTTACAAAGCCTGTGAGCGCAAGAA
CGCGGAGGCGGTGAGGATATTGGTGCGATACAACGCAGACGCCAACCACCGCTGTAAC
AGGGGCTGGACCGCACTGCACGAGTCTGTCTCCCGCAATGACCTGGAGGTCATGGAGA
TCCTAGTGAGTGGCGGGGCCAAGGTGGAGGCCAAGAATGTCTACAGCATCACCCCTTT
GTTTGTGGCTGCCCAGAGTGGGCAGCCTGGAGGCCCTGAGGTTCCTGGCCAAGCATGGT
GCAGACATCAACACGCAGGCCAGTGACATGCATCAGCCCTCTACGAGGCCAGCAAGA
ATGAGCATGAAGACGTGGTAGAGTTTCTTCTCTTCAGGGCGCCGATGCTAACAAAGC
CAACAAGGACGGCCTGCTCCCCCTGCATGTTGCCTCCAAGAAGGGCAACTATAGAATA

FIG 34(I)

GTGCAGATGCTGCTTGCCTGTGACCAGCCGCACGGCGGTGCGCCGTAGCGGCATCAGCC

CGCTGCACCTAGCGGCCGAGCGCAACCACGACGGCGGTGCTGGAGGCGCTGCTGGCCGC

GCGCTTCGACGTGAACGCCACCTCTGGCTCCCGAGCGCGCCCGCCTCTACGAGGACCGC

CGCAGTTCTGCGCTCTACTTCGCTGTGGTCAACAACAATGTGTACGCCACCGAGCTGT

TGCTGCTGGCGGGCGCGGACCCCAACCGCGATGTCATCAGCCCTCTGCTCGTGGCCAT

CCGCCACGGCTGCCTGCGCACCATGCAGCTGCTGTTGGACCATGGCGCCCAACATCGAC

GCCTACATCGCCACTCACCCCACCGCCTTTCCAGCCACCATCATGTTTGCCATGAAGT

GCCTGTCGTTACTCAAGTTCCTTATGGACCTCGGCTGCGATGGCGAGCCCTGCTTCTC

CTGCCTGTACGGCAACGGGCCGCACCACCCGCCCCGCGACCTGGCCGCTTCCACGACG

CACCCGTGGACGACAAGGCACCTAGCGTGGTGCAGTTCTGTGAGTTCCTGTCGGCCCC

GGAAGTGAGCCGCTGGGCGGGACCCATCATCGATGTCCTCCTGGACTATGTGGGCAAC

GTGCAGCCTGTGCTCCCGGCTGAAGGAGCACATCGACAGCTTTGAGGACTGGGCTGTCA

TCAAGGAGAAGGCAGAACCTCCGAGACCTCTGGCTCACCTCTGCCGGCTGCGGTTCG

GAAGGCCATAGGAAAATACCGGATAAAACTCCTGGACACACTGCCGCTTCCCGGCAGG

CTAATCAGATACTTGAAATATGAGAATACACAGTAAccagccctggagaggagatgtgg

ccttcagactgtttccgggacgccccaggtggcctgcatccaggaccccccctgggggtca

gaacaggtgtgaccttgctggtctttttgctggagctttcacccaaaagtgagaacctgat

gtgggagtggacgtggaacctctgctttcacactgtcagcggatcgcagacccgctc

FIG 34(II)

tgcttctggccatagccagagaccttcaacctgggggccagggagagctggtctgggc

aagggtgggcccaggcaggaatcctggccttaaagctggagaacttgtaggaatccctcac

tggaccctcagctttcaggctgcgagggagacgcccagcccaagtatttattttcwcg

tgacacaataacgttgtatcagaaaaaaaaaaaacatgggcgcagcttattccttag

tagggtatttacttgcatgcngcgcttaaagcntactggaaacatgcgttcccnactat

gcttgagaatccccctttgcactggtaaaacgagagccgacgtgcttcaaggttggatttt

tggnttgccccttttggcgttcccgcgggttttgntccgacngtaattgaccccgtgtttt

gtcactttcggagtgttcccgactattgggggggctttttggttgtccccaaaattgtgggt

ggtgtgcggacgccacgagaagtggttcatgggcgataaatcattactgngagaatgta

gagcggcggttttacgaaataatttttttaagccgccttcccaaaa

FIG 34(III)

FIG 35 (I)

FIG 35(II)

FIG 35

h10.1

CCTCCTGAGAGTTCGCCCGGCCCGGGCCCAATGGGnTTGTTCCAAGGGGTCATGCAGAA

ATACAGCAGCAGCTTGTTCAAGACCTCCCAGCTGGCGCCTGCGGACCCCTTGATAAAG

GCCATCAAGGATGnCGATGAAGAGGCCTTGAAGACCATGATCAAGGAAGGGAAGAATC

TCGCAGAGCCCCAACAAGGAGGGCTGGCTGCCCGCTGCACGAGGCCGCATACTATGGCCA

GGTGGGCTGCCTGAAAGTCCTGCAGCGAGCGTACCCAGGGACCATCGACCAGCGCACC

CTGCAGGAGGAAACAGCCGTTTACTTGGCAACGTGCAGGGCCACCTGGACTGTCTCC

TGTCACTGCTCCAAGCAGGGCAGAGCGGGACATCTCCAACAAATCCCGAGAGAnACC

GCTCTACAAAGCCTGTGAGCGCAAGAACGCCGGAAGCCGTGAAGATTCTTGGTGCAGCA

CAACGCAGACACCAACACGCTGCAACCGGGCTG

FIG 35(I)

h10.2

GTGCAGCTCTGCTCGCGGCTGAAGGAACACATCGACAGCTTTGAGGACTGGGCCGTCAT

CAAGGAGAAGGCAGAACCTCCAAGACCTCTGGCTCACCTTTGCCGACTGCGGGTTCGAA

AGGCCATTGGGAAATACCGTATAAAACTCCTAGACACCTTGCCGCTCCCAGGCAGGCTG

ATTAGATACCTGAAATACGACACCCAGTAACTGGGGCCACGGGAGAGGAGGAGTAG

CCCCTCAGACTCTTCTTACTAAGTCTCAGGACGTCGGTGTTCCCAACTCCAAGGGGACC

TGGTGACAGACGAGGCTGCAGGCTGCCTCCCTCTCAGCCTGGACAGCTACCAGGATCTC

ACTGGGTCTCAGGGCCCAGAGCTTTGGCCAGAGCAGAGGAACAGAATGTGTCAAGGAGAA

GAATCATTTGTTTACAAACTGATGAGCAGATCCCAGACCTTCTCTACCTTCAGGAATGG

CAGAAACCTCTATTCCTGGGGCCAGAGGCTTGAGGTGTTCTGGGGAAGGTGGTGC

TCAGAGCCTTCCCTGTGCCCCTCCACTTGTTCTGGAAAACTCACCACTTGACTTCAGAG

CTTTCTCTCCAAAGACTAAGATGAAGACGTGGCCCAAGGTAGGGGGAGCCTG

GGTCTTGGAGGGCTTTGTTAAGTATTAATAAATGTTACACATGTGAAAAAAAAAA

FIG 35(II)

TTGGAGAAGTGTGGTTGGTATTGGGGGCCAATGAATTGGGAAGATGCAGAGATGAAGC
TGAAAGGGAAACCAGATGGTTCTTTCCTGGTACGAGACAGTTCTGATCCTCGTTACAT
CCTGAGCCTCAGTTTCCGATCACAGGGTATCACCCACCACACTAGAATGGAGCACTAC
AGAGGAACCTTCAGCCTGTGGTGTCATCCCAAGTTTGAGGACCGCTGTCAATCTGTTG
TAGAGTTTATTAAGAGAGCCATTATGCACTCCAAGAATGGAAAGTTTTCTCTATTTCTT
AAGATCCAGGGTTCCAGGACTGCCACCAACTCCTGTCCAGCCTGCTCTATCCAGTGTCC
CGATTCAGCAATGTCAAATCCCTCCAGCACCTTTGCAGATTCCGGATACGACAGCTCG
TCAGGATAGATCACATCCCAGATCTCCCACTGCCTAAACCTCTGATCTCTTATATCCG
AAAGTTCTACTACTATGATCCTCAGGAAGAGGTATACCTGTCTCTAAAGGAAGCGCAGCGT
CAGTTTCCAAACAGAAGCAAGAGGTGGAACCCTCCACGTAGCGAGGGCTCCCTGCTG
GTCACCACCAAGGGCATTTGGTTGCCAAGCTCCAGCTTTGAagaaccaaaattaagcta
ccatgaaaagaaggaggaaaagtgagggaacaggaaaggttgggattcctctgtgcagaga
ctttggttccccacgcaagccctgggggcttggaagaagcacatgaccgtactctgcgt
ggggctcccacctcacacccacccctgggcatctttaggactggaggggctccttggaaa
actggaagaagtctcaacactgttttctttttca

FIG 36A

....LEKCGWYWGPMNWEDAEMKLKGKPDGSFLVRDSSDPRYILSLSFRSQGITHHTR
MEHYRGTFSLWCHPKFEDRCQSVVEFIKRAIMHSKNGKFLYFLRSRVPGLPPTPVQLL
YPVSRFSNVKSLQHLCRFRIRQLVRIDHLPDLPLPKPLLSYIRKFYYYDPQEEVYLSL
KEAQRQFPNRSKRWNPPRSEGLPAGHHQGHLVAKLQL*

FIG 36B

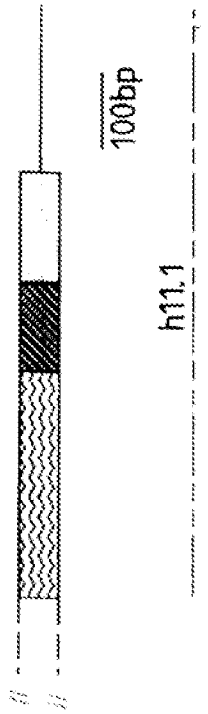
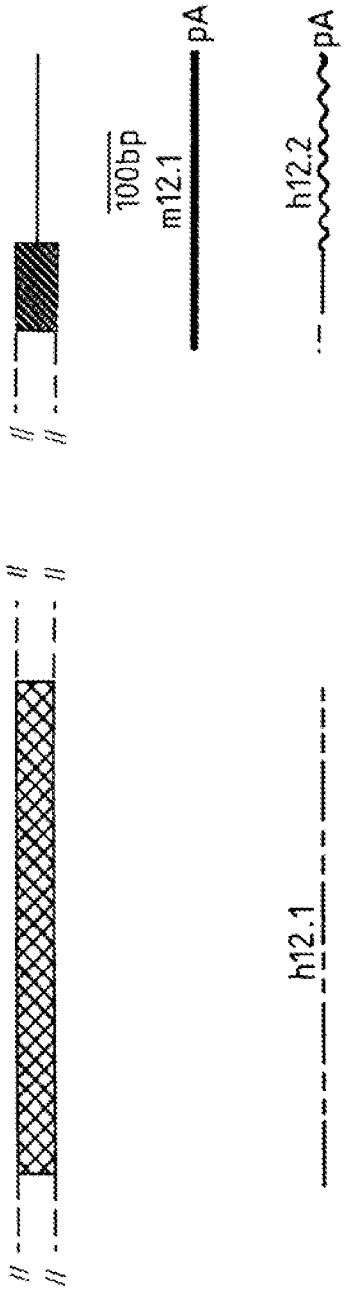


FIG 37

FIG 38



GTTCCAAGCCTAACCCATCTTTGTCGTTTGGAAATTCGGGCCAGTCTAAAAGCAGAGC

ACCTTCACTCTCTGACATTTTTCATCCATCAGTTGCCACTTCCCAGAAGTCTGCAGAACTA

TTTGCTCTATGAAGAGAGGTTTTTAAGAATGAATGAGATTCTAGAACCAGCAGCTAATCAG

GATGGAGAAACCAGCAAGGCCACCTGAcacaggtcctttaatttctgttttagtcacaaaa

agacggcttgtgtgactgtttggatttggtgatcaaaatgtccatgtttacagtttgctt

ttcccagtttgtgtctttcccaatattgtgaaccttatccatctttgccttactcagtt

ttatttctagtgcacttttgttgtattatttgtttacctgaccatttttctactttat

tctgctaataaaactgtaattctgaaaaaaaaaaaaaaaaaaaaaaaaaaaaaaaaa

FIG 39

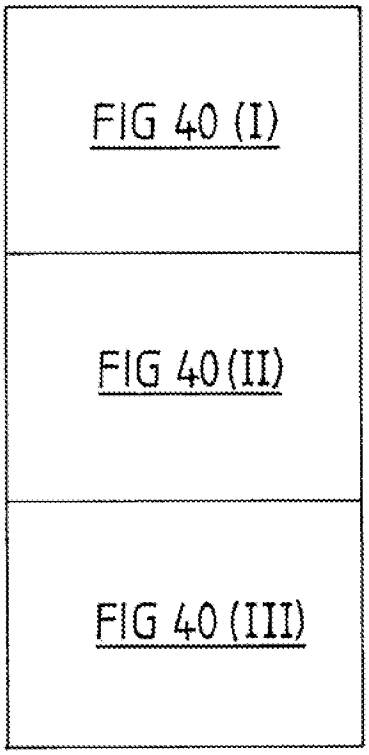


FIG 40

h12.1

GGGGATCGAAAGCGGGGGGCTTCTGGGACGCAGCTCTGGAGACGCGGCCTCGGACCAGC

CATTTCGGTGTAGAAGTGGCAGCACGGCAGACTGGTCAAACAAATGGATTTTACAGAG

GCTTACGCGGACACGTGCTCTACAGTTGGACTTGCTGCCAGGGAAGGCAATGTTAAAG

TCTTAAGGAAACTGCTCAAAAAGGGCCGAAGTGTCGATGTTGCTGATAACAGGGGATG

GATGCCAATTCATGAAGCAGCTTATCACAACTCTGTAGAATGTTTGCAAATGTTAATT

AATGCAGATTCATCTGAAAACTACATTAAGATGAAGACCTTTGAAGGTTTCTGTGCTT

TGCATCTCGCTGCAAGTCAAGGACATTGGAAAATCGTACAGATTCTTTTAGAAGCTGG

GGCAGATCCTAATGCAACTACTTTAGAAGAAACGACACCATTGTTTTTAGCTGTTTGAA

AATGGACAGATAGATGTGTTAAGGCTGTTGCTTCAACACGGAGCAAATGTTAATGGAT

CCCATTCTATGTGTGGATGGAACTCCTTGCACCAGGCTTCTTTTTCAGGAAAATGCTGA

GATCATAAAATTGCTTCTTAGAAAAGGAGCAAACAAGGAATGCCAGGATGACTTTTGGA

ATCACACCTTTATTTGTGGCTGCTCAGTATGGCCAAGCTAGAAGCTTTGAAGCATAC

TTATTTCATCCGGGTGCAAATGTCAATTGTCAAGCCTTGGACAAAGCTACC

FIG 40 (I)

h12.2

CACAAATGGGACCATACAAAAATCTTGTTAATAACCACTTNACTAACCGGG

ACCTGTGACACTGGGNCTAAACAAAGTAAGTCCCTGTTTACTCAGNCAGTGTTTGGGG

GACATGAAGGATTGCCTAGNAAATATTACTCCGGAATGGTCTACAGCCCACGNACGCCC

AGGCGTGCCTTGTTTTTTGGATTCAGTTCTCCTGTGTGCATGGCTTTCCAAAAGGAGGT

GGAGCTGTRAGTTCTTTGGAATTGTGAACATTCTTTTTGAAATATGGAGCCCAGATAAA

TGAACTTCATTTGGCATACTGCCTGAAGTACGAGAAGTTTTTCGATATTTCGCTACTTT

TTGAGGAAAGGTTGCTCATTGGGACCATGGAACCATATATATGAATTTGTAAATCATG

CAATTAAAGCACAAGCAAAATATAAGGAGTGGTTGCCACATCTTCTGGTTGCTGGATT

TGACCCACTGATTCTACTGTGCAATTCTTGGATTGACTCAGTCAGCATTGACACCCTT

ATCTTCACTTTGGAGTTTTACTAATTGGAAGACACTTGCACCAGCTGTTGAAAGGATGC

TCTCTGCTCGTGCCTCAAACGCTTGGATTCTACAGCAACATATTGCCCACTGTTCCAT

CCCTGACCCATCTTTGTCGTTTGGAAATTCGGTCCAGTCTAAAATCAGAACGTCTACG

GTCTGACAGTTATATTAGTCAGCTGCCACTTCCCAGAAGCCTACATAATTATTTGCTC

TATGAAGACCGTTCTGAGGATGTATGAAGTTCCAGAACTGGCAGCTATTCAAGATGGAT

AAATCAGTGAAACTACTTAACACAGCTAATTTTTTTCTCTGAAAAATCATCGAGACAA

FIG 40 (II)

AAGAGCCACAGAGTACAAGTTTTTATGATTTTATAGTCAAAAGATGATTATTGATTGT

CAGATAGGTTAGGTTTTTGGGGGGCCAGTAGTTCAGTGAGAATGTTTATGTTTACAACT

AGCCTTCCCAGTAAAAAAAAAAAAAAAAAAAAAAAAA

FIG 40 (III)

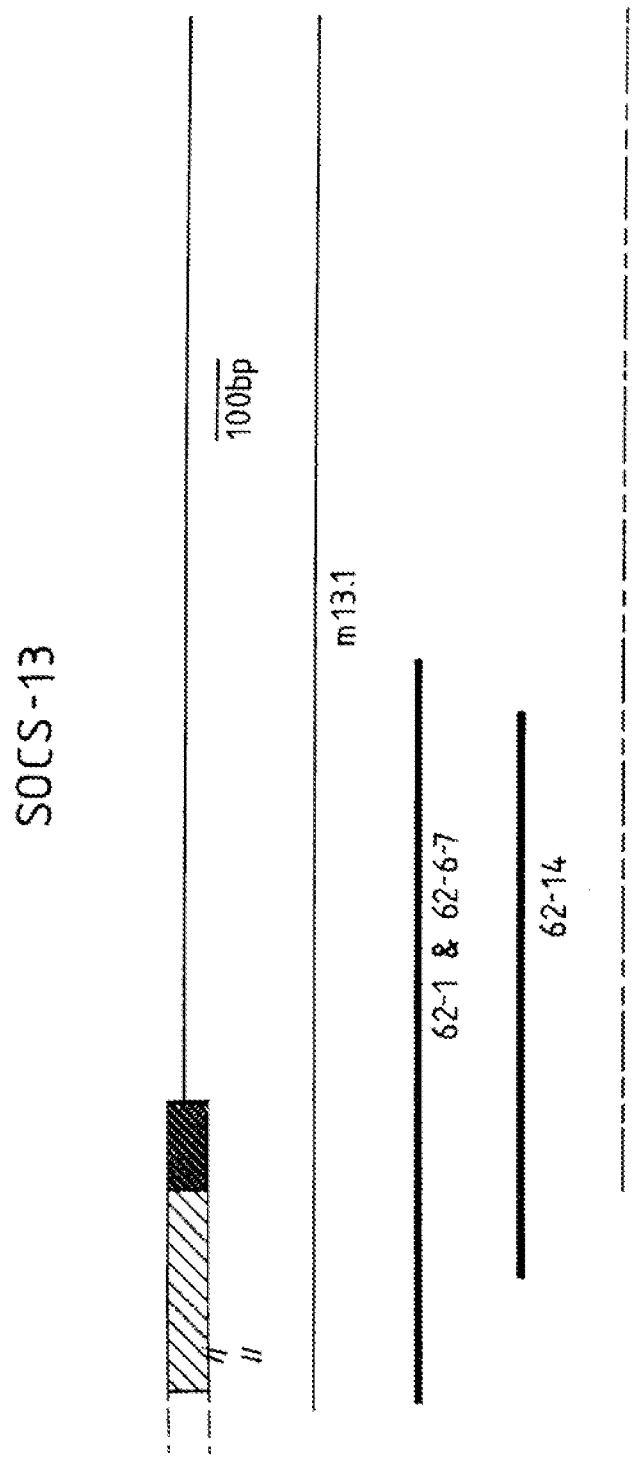


FIG 41

FIG 42A (I)

FIG 42A (II)

FIG 42A

CGGGGGGGCTGGGACCTGGGGCGTAACCGTCTCTACCACGACGGCAAGAACCAGCCAAG

TAAAACATACCCAGCCTTTCTGGAGCCCGGACGAGACATTCATTGTCCCTGACTCCTTT

TTCGTGGCCCTGGACATGRATGATGGGACCTTAAGTTTCATCGTGGATGGACAGTACA

TGGGAGTGGCTTTCCGGGGACTCAAGGGTAAAAAGCTGTATCCTGTAGTGAGTGCCGT

CTGGGGCCACTGTGAGATCCGCATGCGCTACTTGAACGGACTTGATCCTGAGCCCCTG

CCACTCATGGACCTGTGCCGGCGTTCGGTGCGCCTAGCGCTGGGAAAGAGCGCCTGG

GTGCCATCCCCGCTCTGCCGCTACCTGCCTCCCTCAAAGCCTACCTCCTCTACCAGTG

Atccacatcccaggaccgccatacgacagccatctggtgccaartcactgagccccgtt

ggggtccgccgacccctgcgcctgggatggaygcccacctcagcccatgggcagacgtg

ccccctcatcctaccggctgcctgctgggggaacctatgccaacggacttctccct

tcccaacactggctgaagcagcagcacccagggccctttccctgaaccagatgcagagaa

taaactatgaaaaacctctctcaggcgccttctgctcctcaggtggagtgggctgcccccc

cactcctctgcagagagaggaggctacacccacctgggggtccctgggaggtaagactagta

ggaggtgccagggctgartcccaaaagcaggaatggccaggamcaggccatacagatga

agctcaggatgtcacataccatggacamtgagacagaaccccaggttggamttcccttt

gggccaacgagtgccagctttaatgtcagctgctgtggcctgtatttatt

cttaaacagtagcaaaggccatttattttccactttagaaaggaaaccttgggtggg

tggyttcccctcgatgtgctttccccacctccctggaatgtgtgtgccacacctgtcc

FIG 42A(I)

ttgtcccaggccaggactgtggtgtgcacagatacacgtatgtcgt
cgtgcatgaccccctgactagttcctaagtagccctgcaccaagcaccagagcagaccc
caagaggaggcccgtgcaagtcccccatgtcccaggtccttctgcttctgttgcctttggga
ctcatacaccggcacacgtgtttcagcctcttgacttccatgagcttcgaatttttgcc
cccgattcttctgatatttcccctcccattggcatcctcccaaagctcctgggaggcctggagggcat
taggacacatggaatgagtgggggtctccagccccctgggaaagccactggcaaggcagg
attagaaagaccaagagcagggtgggggcgccatgaagcctgtatgccctctcaggctca
agacccccgccacacacccactcaagccctcagaagtggtgtgtagggcagccccaggag
aggaatgccctgtcctagcagcacgtacatgggagcacccccacatgtgctcccagccctct
ggctgtttctcttgctctagaatcaactcccctacattgggaatgtagccatttgggtag
aggacttgccctagcctgcaggaagctcacgttcccatcccccctgcaccaaggagaatcaa
agctcaggaggctgaggcaggaggattgctgtcagtgggtgtacagaggtcatggccat
cctgggctatattaaaccctttgtcctttaagaaaaaagaaaatcaactttccattga
atctgagttctgctcatttctgcacaggtacaaatagatgacttkattttgttgaaaaat
gkttaatatatttacmtatatatttgtaagaagcatt

FIG 42A(II)

....GGWDLGRNRLYHDGKNQPSKTYPAFLEPDETFIVPDSFFVALDMXDGTLSFIVD

GQYMGVAFRGLKGKKLYPVVSAVWGHCEIRMRYLNGLDPEPLPLMDLCRRSVRLALGK

ERLGAIPALPLPASLKAYLLYQ*

FIG 42B

AAGGGTAAAAAACTGTATCCTGTAGTGAGTGCCGTCTGGGGCCACTGTNAGATCCGAA

TGCGCTACTTGAACGGACTCGATCCCGAGACNTGCCGCTCATGGATTTGTGCCGTCGC

TCGGTGCGCCTGGCCCTGGGGAGCGCCTGGGGGAGAACCANCNACCTGCCGCTG

CCGGCTTCCCTCAAGGCCTACCTCCTCTACCAGTGACGTTCGCCATCATACCGCCAGC

GCGACAGCCACCTGGTGCCAACTCACTGAGCCGCCTG

FIG 43

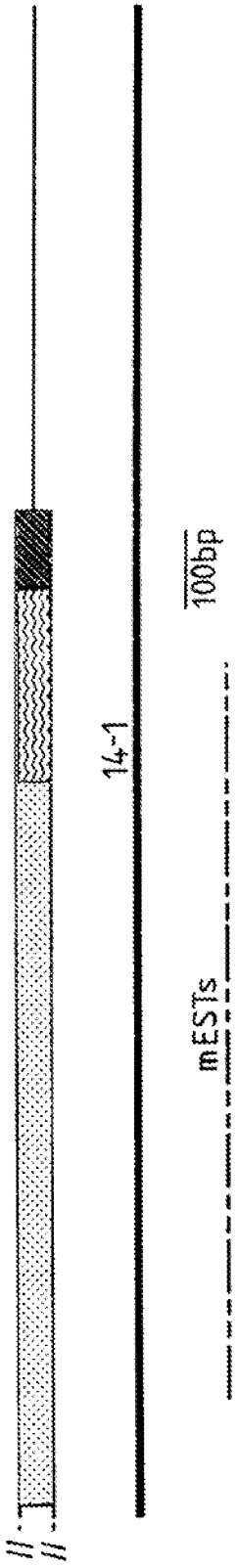


FIG 44

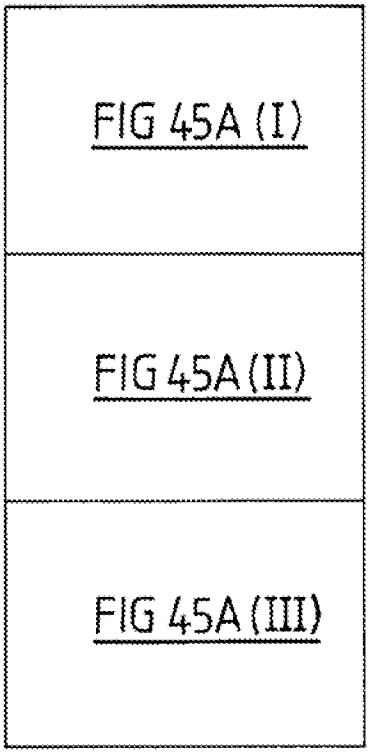


FIG 45A

```
. . . . AAGTGGCGGCGGTCCCTGGAGAGGCAGGCGGAGGCAGCGGCAAGTCTGACTCTGG
GCTGACCGTGGAGCCGGGGCGGGGCTGACAGCCAGGCCTCCGCCTGGCGGGAGCCGC
ACGAGGAGCGGGAGTGGCCGGGCCTCTCTTCCGCGCTTGAGCGAGCGCCGGGTGATGG
CGGTGGTGATGGCGGCAGGCGCTCCGGACAGCTCCGCTTGAGCTGAGGCTCGGAGAGATC
CGTCCAGAAAGTGCCCAGAAGAAACTTCCTCTTAGAAAAGCTGAAAAACACARTATTT
ATAACACTGGAAATTGTAAAGAATTTGTTTAAAATGGCTGAAAACAATAGTAAAAATG
TAGATGTACGGCCTAAAACAAGTCGGAGTCGAAGTGCTGACAGGAAGGATGGTTATGT
GTGGAGTGGAAAGAAGTTGTCTTGGTCCAAAAAGAGTGAGAGTTGTTCTGAATCTGAA
GCCATAGGTACTGTTGAGAATGTTGAAATTCCTCTAAGAAGCCAAGAAAGGCAGCTTA
GCTGTTCGTCCATTGAGTTGGACTTAGATCATTCCTGTGGGCATAGATTTTTTAGGCCG
ATCCCTTAAACAGAAACTGCAAGATGCGGTGGGGCAGTGTGTTTTCCAATAAAGAATTGT
AGTGGCCGACACTCTCTCCAGGGCTTCCATCTAAAAGAAAGATTCATATCAGTGAACTCA
TGTTAGATAAGTGCCCTTTCCCACCTCGCTCAGATTTTAGCCTTTTAGGTGGCATTTTAT
TAAACGACACACTGTGTTCCTATGAGTCCCAACTCAGATGAATGGGTGAGTGCAGACCTG
TCTGAGAGGAAACTGAGAGATGCTCAGCTGAAACGAAGAAACACAGAAGATGACATAC
CCTGTTTTCTCACATACCAATGGCCCAGCCTTGTGTCATAACTGCCAACAGTGCTTCGTG
TACAGGTGGTCACATAACTGGTTCTATGATGAACTTTGGTCACAAACAACAGCATAGAA
GACAGTGACATGGATTCAGAGGATGAAATTATAACGCTGTGCACAAGCTCCAGAAAAA
```

FIG 45A(I)

GGAATAAGCCCAGGTGGGAAATGGAAGAGGAGATCCTGCAGTTGGAGGCACCTCCTAA

GTTCCACACCCAGATCGACTACGTCCACTGCCTTGTTCCAGACCTCCTTCAGATCAGT

AACAATCCGTGCTACTGGGGTGTCATGGACAAAATATGCAGCCGAAGCTCTGCTGGAAG

GAAAGCCAGAGGGCACCTTTTTACTTCGAGATTCAGCGGCAGGAAGATTATTTATTCTC

TGTTAGTTTTTAGACGCTACAGTCGTTCTCTTCATGCTAGAATTGAGCAGTGGAATCAT

AACTTTAGCTTTGATGCCCATGATCCTTGTGTCTTCCATTCTCCTGATATTACTGGGC

TCCTGGAACACTATAAGGACCCCAGTGCCTGTATGTTCTTTGAGCCGCTCTTGTCCAC

TCCCTTAATCCGGACGTTCCCCTTTTCCTTGCAGCATATTTGCAGAACGGTTATTTGT

AATTGTACGACTTTACGATGGCATCGATGCCCTTCCCATTCCTTCGCCTATGAAATTGT

ATCTGAAGGAATACCATTATAAATCAAAAGTTAGGTTACTCAGGATTGATGCCAGA

GCAGCAGTGAtgcggagaggttagaatgtcgacctgcatacatatttcatttaatat

ttatttttcttatgcctctttgaatttttgtacaaaggcagttgaatcaaataaaac

tgtgccctaagttttaattcccagatcaatttatttttttatgatacacttgttatat

attttaagcaggtgtttggttttgtttaccatataaatttacatatggtccaggc

atatttacaattcaaggcattgcatatacatttgaatattctgtatttttaaataa

tcttttgttcttcctatgtgtgaaaatatttttgctaatctatgcttatcagtattcttg

tatgaccgaatagttacctattcctttttcatcttgaagatttttcagtaaagagtgtt

gtaatcaatccattataaatgtaatttgacttttgtaatttgccaataggagtgtttaaac

FIG 45A(II)

aacaaaaatgatttaaaatgaaacttaaatgtatttttcatttttaaaatatttaaactaaaacca

agtttgttttgttagtttatttctagccaataaagaaaaagagaatgtagcatcctagaggtg

tatttgttctgcagtttggcaggaccgtcagttagtccaaataaaacatccccctcagccg

tggaggcgaatggaacctgtgctcctttctttacgggaagctttgcaaagcaaaaatagc

agggttacaaagctttggagttgttaagggcaaactagagttttctctatttttatagac

tgttgttgcacctacttagctctttttttggggaactcctagttcccaggggaaaatacct

cgtgcc

FIG 45A(IIII)

....SGGGPWRAGGGSGKSDSGLTVEPGRGLTARPPPGGSRTRSGSGRASLPRLSERR

VMAVVMAAGARTAPLELSSERSVQKVPRRNFLLEKLKNTXFITLEIVKNLFKMAENNS

KNVDVRPKTSRSRSADRKDGYVWSGKKLSWSKKSESCSESEAIGTVENVEIPLRSQER

QLSCSSIELDLDHSCGHRFLGRSLKQKLQDAVGQCFPIKNCSGRHSPGLPSKRKIHIS

ELMLDKCPFPPRSDLAFRWHFIKRHTVPMSPNSDEWVSADLSERKLRDAQLKRRNTED

DIPCFSHITNGQPCVITANSASCTGGHITGSMMNLVTNNSIEDSDMDSEDEITTLCTSS

RKRNKPRWEMEEEILQLEAPPKFHTQIDYVHCLVPDLLQISNNPCYWGVMDKYAAEAL

LEGKPEGTFLLRDSAQEDYLFSVSFRRYSRSLHARIEQWNHNFSFDAHDPCVFHSPDI

TGLLEHYKDPSACMFFEPLLSTPLIRTFPFSLQHICRTVICNCTTYDGIDALPIPSPM

KLYLKEYHYKSKVRLLRIDVPEQQ*

FIG 45B

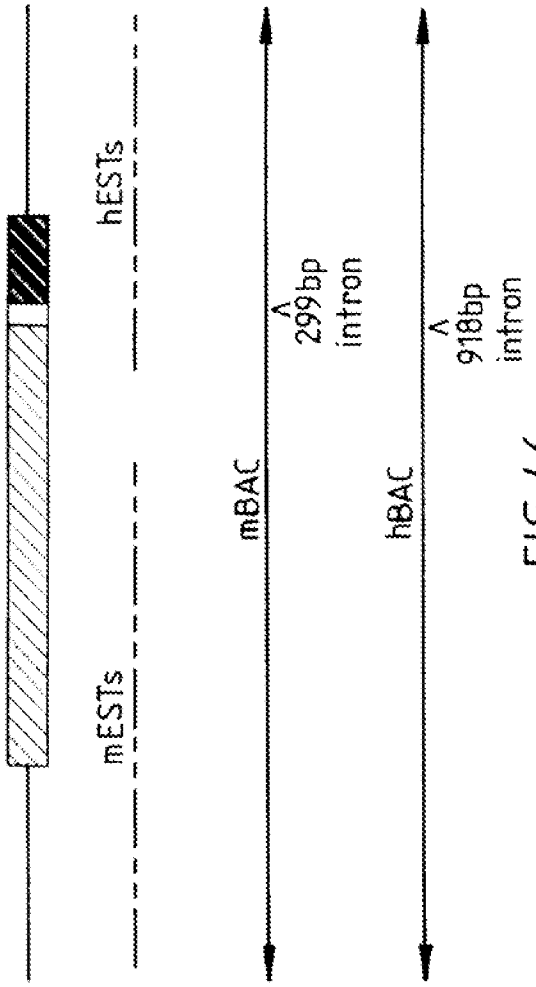


FIG 46

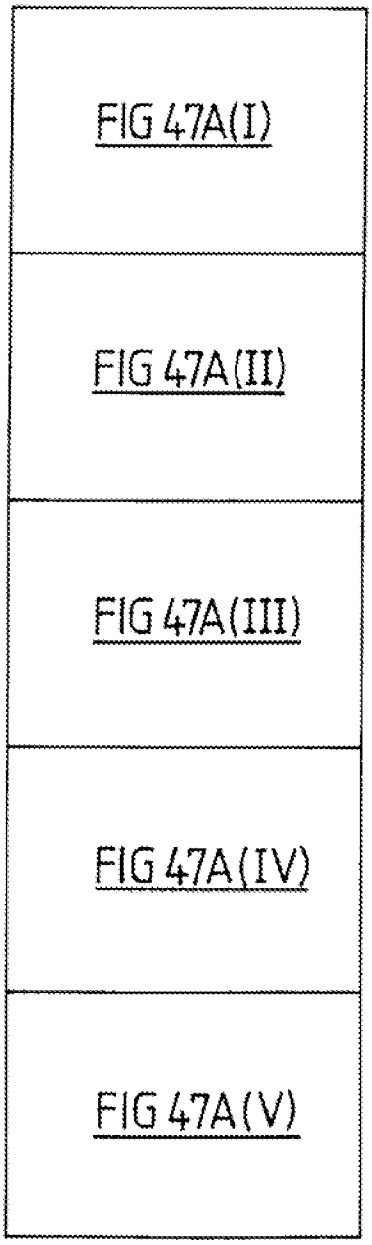


FIG 47A

```
ccctctgggcaagccgccccccccccacccatctaccacacacacacacacacacaca
cacacacattcagaccttggggcaaaaacaaagcaaaataacaacaacaaaaacactg
cctgtggaaagtccttacttcaggaaggttggcagatgaggagcaagggaacatttta
tcaggactgccacaaaggagtcttttttttttaatggttttcaagacagggtttctct
gtatagccctggctgtcctggagctcactttgtagaccaggctggcctcgaactcaga
aattcgcctgcctctgcctcctgagtgctgggattaaaggcgtgcagcaccatgtcca
actggcattttctcaattaaggttcgttcctttcagataactctaggttctgggtcaa
gctgacacaaggctacacagcacagtttgtatgccacattcagttcagaagacaccca
acctccctggaactggaacttatgcacatttgtgagcttccacttgggagtgggaacc
tgaactgggtcctctgcaagagcagccgtgctcttaactgctgagccatttcagcagc
ctcacatcagaattaagttaaaattagccgggtatgaatcatacccttagaatcctag
catctgaaagcagagctaagagaaacagggattcaagaccagctcttggctacagagc
ccgtcctgtcctaggatgggctacaagagactatttcaaagccatccaaacaacaata
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atgggatttttttgggataaggtttctctgtctagccctggcatagattcactctgta
```

FIG 47A(I)

gactaggctagccttgaactcagagatccgcctgcctctgcctcccaagtgctgggat
tataggtgttgcaccaccaccactgcccagccaccactttgggatttttgaactgttatcaaga
ggctttcgaggaggtcaaacttcaacagcaacctctccatgataatgtagctaatgatc
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ggagttcaggaagggtgtcaaggccgcttactgatctttagggcctcaggaatgactag
ctcaggcagagagagcaaaggtctccagtggagaagtctacacacacacacacaca
cacacacacacacacacagaatccaaggcgatgacgtcatcaaagggttaattc
tagtctgggatgggggggagggtgggggcacgcagcctgtcaggtggctttggaaaaata
aactgctgaagagtctgacgcccagggagtcctgggaggacaagaggttacccactca
aagagtgtgctcccacaaagcatgcgcgccttgtccacgtctggagtcgtcacttattt
ttgccctggatttcttgtagcccggtgggttcctcaaggcggtaagtggtgtggccgccgt
ggtctgggaggtgacgatagggttaatcgtccacagagcccagggggcgggagcgcgggc
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ttccctatctgtacttcccacagaggtctctgcgagctagggggacagtgagggtgcgggg
gtagggggcccggcgttagagccagcaaggggacggttcacggtaaggtctgagggaga
gagagcctccctgagaaaacttgggggggcgcgacacacagatagggtgaaagcagagtgatag

FIG 47A(II)

acctgggatggttagggaccaaggaagaccaggctggttggcataccaccggtgaac

ggatgggagtcctagggaaagatgatgcgccctaacagtcctttctgtcctccacaccac

tccagggacgatccggagctcaacttttcaaaaagcgagacgccccagcaagcctgtttt

tgagaagtttcttcagcggctctcctcATGGGCCAGACGGCCCTGGCAAGGGCAGCAG

CAGCACCCCTACCTCGCAGGCTCTGTACTTCTCTCCCTCCCGAGGGCTTGGAG

GAGCTCCTGTCTGCTCCCCCTCCTGACCTGGTTGCCCAACGGCACCACGGCTGGAACC

CCAAGGATTTGCTCCCGAGAACATCGATGTCAAGGAAGGGGGGTCTGTGCTTTGAGCGGCG

CCCTGTGGCCCCAGAGGCACTGATGGAGTCCGGGGGAAAACGGGGGCTATTTCGAGAGGTCTG

CACGGCCTGGGAGATCAGCTGGCCCCCTGGAGGCAAAGGGGGCACACACGCCGTGGTGGGCG

TGGCCACCGCGCCCTCGCCCCGCTGACCACTATGCGGCGCTTTTTGGGCAGCAA

CAGCGAGTCCTGGGGCTGGGATATTGGGCGGGGAAAATTGTATCATCAGAGTAAGGGC

CTCGAGGCCCCCCCAGTATCCAGCTGGACCTCAGGGTGAGCAGCTAGTGGTGCCAGAGA

GACTGCTGGTGGTTCTGGACATGGAGGAGGGGACTCTTGGCTACTCTATTGGGGGCAC

GTACCTGGGACCAGCCTTCCGTGGACTGAAGGGGAGGACCCTCTATCCCTCTGTAAGT

GCTGTTTGGGGCCAGTGCCAGGTCCGCATCCGCTACATGGGCGAAAGAAGAGgtgaga

tacggactaggtgtgggagatcactacttgggcaatggtttgggctggaaaactcat

ggttggagcacaggaagtaggcttcttgtcactttggcctgtcacttagatggcctttg

gatctagcttcactcccaatcccctattggatgtgatgcacaaattcagagccctttggg

FIG 47A(III)

tctccctcagctgaggtggcggtggaaatggaggaagaaggaagggtgcctgagcagg
atctcaagtttcaaggatgccctggagttgcttactttcctttctcctccg
cagTGGAGGAACCACACAATCCCTTCTGCACCTGAGCCCGCCTGTGTGTGCGCCATGCTCT
GGGGGACACACCCGGCTGGGTCAAATATCCACTCTGCCTTTGCCCCCTGCCATGAAGCGC
TATCTGCTCTCTACAAATGAcccagtagtacagggtgtgctggcaccctaccgtgggggac
aggtggagaggcacccgctggcctagacaacttttaaaaaagctggtgaaggctgggggggg
gggggctggaccccctttcacctcccctttctcacaggagcaagacatatagaaaatgatat
taaacaccatggcagcctgggacaaagaggtttttgaagtaaaaaaatgagatgtattg
tcacaaaccctgtttcattattgttttttgttttacactccccccaccccaggccta
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tatttcccctttacatggtaggatgggttcacaaaacacaatacagggggctttggcaccgtgg
gggagggggactatcccagggccctcttagggtctcatgtataccgaatttcagaccccgaaa
gctctgaaatttctgcatcagacatccagtagaacttgggagtgaaggctagaggccaaggg
ccatctaaggtgacagggccaaaagtgacacgaaggcccacttcctgtgctccaaccatgag
ttttccagcccaaaaccaatggaaggtgatttcacttgtcagggcccaaagggacagtca
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aagtggtaaaggggatttggccctggtcccaaccataatagggcggtgggaaacgggctcagg
agggtacagcgtggattagggccacaagatgatgtcatcagaagcatgtg

FIG 47A(IV)

accggtgggagcagttactaaaacttctgggcaacctagtccatgctatgcaggcaggt

agagggatgggcagtgctcattgtttggcattgatgtccacaaattcaggcttga

gagatgcgccacccacaaggaagccgtccacgtcaggctggcttgccagctctttgca

ggttgctccagtcacagaacctgtaccaggaacaagaagacagtttggtcaggtctat

gatcagaacacttaagccccacctctctgtgcaaggcagcctcagtctgtctttagccc

atttccgtcttagctagagccaaagccactcacctcccataaaatgatccgggtgctctg

agccacccccatcattgacatttggatttcagccatccccgggagcttctcgtgtacttcc

tgtgccctagaaggaggaggcagagctactaagtaagctcctttcctatctatcattcaa

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gagagtggcaaggctcccaccaccaggcttggaatgaacatttttggcaaagtcac

tctccttggtgagtttgggggccctctgtctctaaaggggcttggatgggctcccatag

ctgtgtgagtctgtttaaagccgggacaggctctgggtagttaccctgctgag

gggttgccgtctttgccagtcccaatgggcccacacaggttcataggccaggaccacctt

gctccagtctttcacatttatctgtgggggcagaggaggagtgagtaggaaggagctga

cccgcccaagc

FIG 47A(V)

MGQTALARGSSSTPTSQALYSDFSPPEGLEELLSAPPPDLVAQRHHGWNPKDCSENID

VKEGGLCFERRPVAQSTDGVRGKRGYSRGLHAWEISWPLEQRGTHAVVGVATALAPLQ

ADHYAALLGSNSESWGWDIGRGKLYHQSKGLEAPQYPAGPQGEQLVVPERLLVVLDME

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FIG 47B

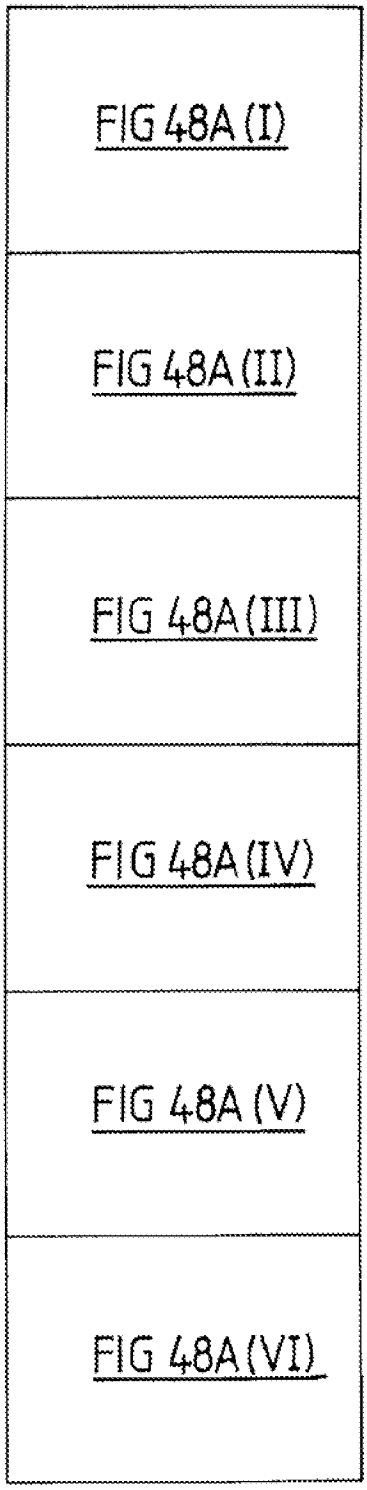

FIG 48A

gtacttcttttatatcctccataatttttatttactatattacatgatacattatttta
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atcattaaaatgcgaaccagaaactcttccaaaatgtgttacatctataacctcattgga
ttctcactaccaaccccatgcaatagatactaatgtgatctctgtctttacagaggaag
aaacaggcacagggaggttcagtaatttgccccaaggtcatacacacactggccttcag
gtattcatgccccgggagtcctggtcccacagctggcatgtttgccattatattatt
gcctccttatagtgtcgggcactcattaagcacattgacagctatgcttggtgagtgac
tactatgtacccagctctgtgctacatgcttttacctggattatttcaactgcacaaca
accctgtgagggtaaactaccatcattgctcctatttttacataaacagaaaactacagaaa
tctgggggctgggcgtagtggcctcatgcctgaaatcccagcacttttgggagaccctgtc
tctaaaaaaaaatttttttttggccggacgttgggtggctcacacctgtaatctcagcact
ttgggaggctaaggcaggcagatcacaaggtcaggagttctagaccagcctggccaac
atggcaaaaccctgtgtctactaaaaaatacaaaaaattagctaggcgtggtggcaggtg
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gactctgtctcgaaaaaaaaataaaaaaataaaaaatattttttaaaaaattagctg
ggtgtggtagcacatgcctgtagtcccagctacttgggaggctgaggtaggaggatca
cttgagcccaggaggtcaaggctgcagtgggctgtgatggcgccactgcactctagcc

FIG 48A(I)

ttggtgacagcaagaccctgtctcaaaaaaaaaaaaagagaaatcgggcaacttccc

caagatcgcgcagtttaaactagtggcatagcttcactcaaaactcgaagtctttaatcagg

acactctaccaaaatgagatcaacggcctcagtaaatggattggcatccagtatgaagact

ggaccagcagcagggagaactatgatgcgtacagcctagagcctgaagcagatttcacagc

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gcgagtaagggggatggtccatgctgagggcccaaatgggggcgaactcgcgagagtctc

tggcgacctggatcagatgggcgagggcgcagatgaagggcccaggagcttttgggggcag

FIG 48A(II)

cgaggagggaggagcgggcccgttggcaaacttgggtgaaaggatgggtaccctgggt

gacgagccccccgccaggatttctgctcttcacgcccctttttctcccagctcccttccag

gtcaatcccaaactggagctcaacttttcagaagagaaagacgccccagcaagccctctt

cgggagtcctctagctcctcaccctccATGGGCCAGACAGCTCTGGCAGGGGGGCAGCA

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cagtgctgggaaaggctagggggtcttcacagctgttatttaatttaacccaacagcaa

FIG 48A(III)

tagaggtgaaacaggcttgagaaagcaacttctcaagttctcttggccagtaaatgg

tgaaccttcagaatggagggaggaactgcagggatgagagaattcaggagatatcaac

ccctgagcaagaggtgcaaaagcgttaggtactgggtttgatgtacaggtccaaaagaa

ggatgggcagagccaggtacccaggctgtataccggatttccctgggctctaacctgtc

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tgggaggcagaacttcccgggtatctcaaaattcccctttcagccaggtgggcacactcg

aagcaggaaaggcagaaaaggcatcttgagtaggaccccgtagtttgaggacatctggctg

gtggctgcacccatacttacattcccctcctctctcccagCGGAGCCACACTCCC

TTCTGCACCTGAGCCGCCTGTGTGTGGCGCCACAACCTGGGGGCATACCCGGCTCGGCCA

GGTGTCTGCCCTGCCCTTGCCCCCTGCCATGAAGCGCTACCTGCTCTACCAGTGAgcc

ctgtgataccacagactgtgctgaggtctttgccaccaccccctcccccttgggggaggtgg

ggaggcactgcctggcctagaccagctgctgaaaggctggtgagggctgagccccctacccc

aacccaagctctgcggaaatcaacagccccagagcccacttggagggaggaaagaaagggg

FIG 48A (IV)

FIG 48A(V)

agccggcgttcaaggctatgacagtctgctacgcaaaacatttttttcaagtaaaaata

gtaagagatgttgttatagaaacctgttcttgttttttttttctttgcacaaatga

tcatttatagctgcctcaaaaaggaagatttatctgggcaagtccagtgaaggcaga

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cattacagggtgaagatataaacagtaaaggaagatacagtttggatgaggccacagg

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gcagagatacagatgggagggaaggggtgaacaagaaagagctctcccagccaggttctcc

ggagtacgaagaacggtggccctactgccccccctagtggacattgggggg

FIG 48A(VI)

MGQTALAGGSSSTPTPQALYPDLSCPEGLEELLSAPPPDLGAQRRHGWNPKDCSENIE

VKEGGLYFERRPVAQSTDGARGKRGYSRGLHAWEISWPLEQRGTHAVVGVATALAPLQ

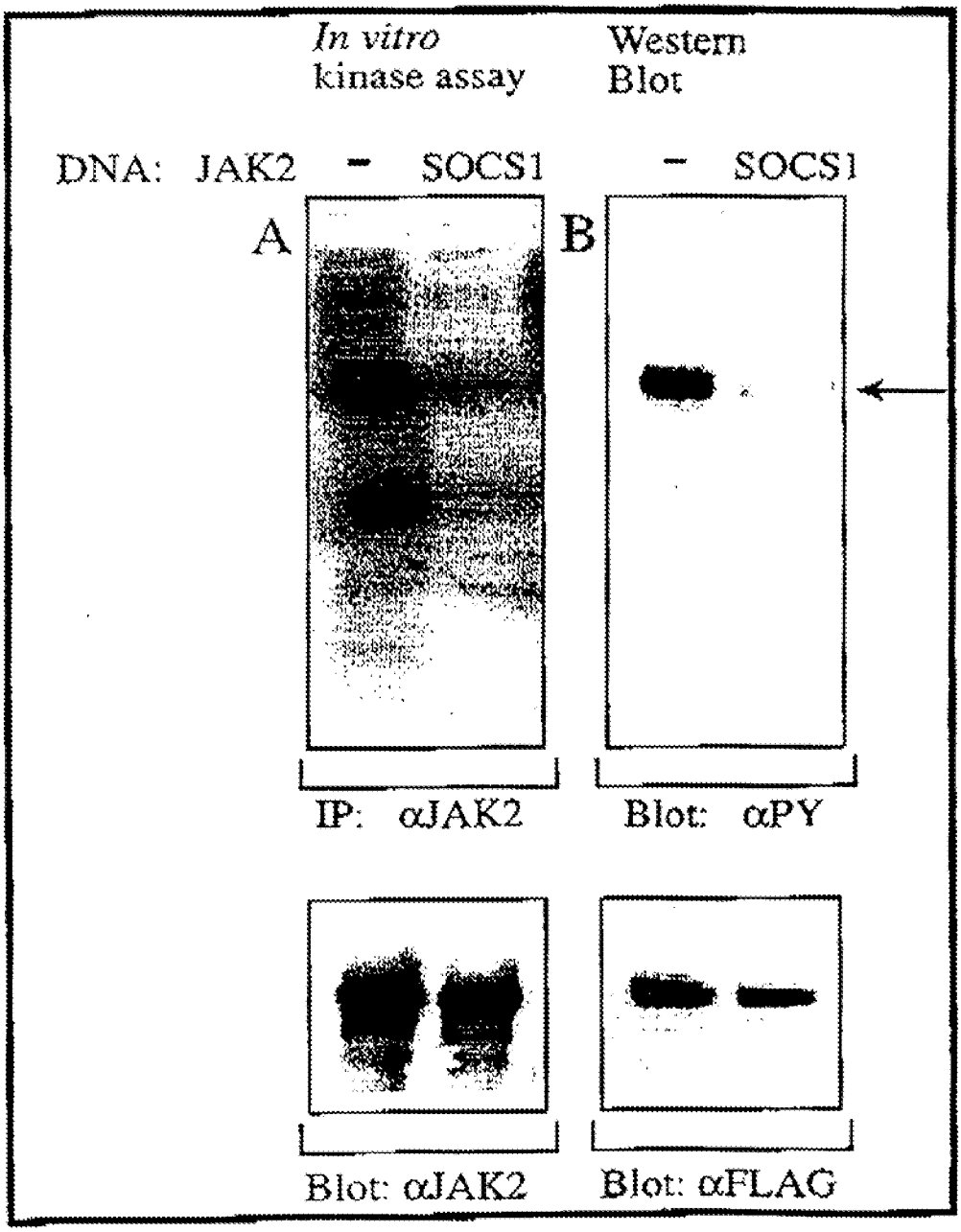
TDHYAALLGSNSESWGWDIGRGKLYHQSKGPGAPQYPAGTQGEQLEVPERLLVVLDME

EGTLGYAIGGTYLGPAFRGLKGRTLYPAVSAVWGQCQVRIRYLGERRAEPHSLLHLSR

LCVRHNLGDTRLGQVSALPLPPAMKRYLLYQ

FIG 48B

FIG 49


In vitro
kinase assay
Western
Blot
DNA: JAK2 - SOCS1 - SOCS1
A
B
IP: αJAK2
Blot: αPY
Blot: αJAK2
Blot: αFLAG

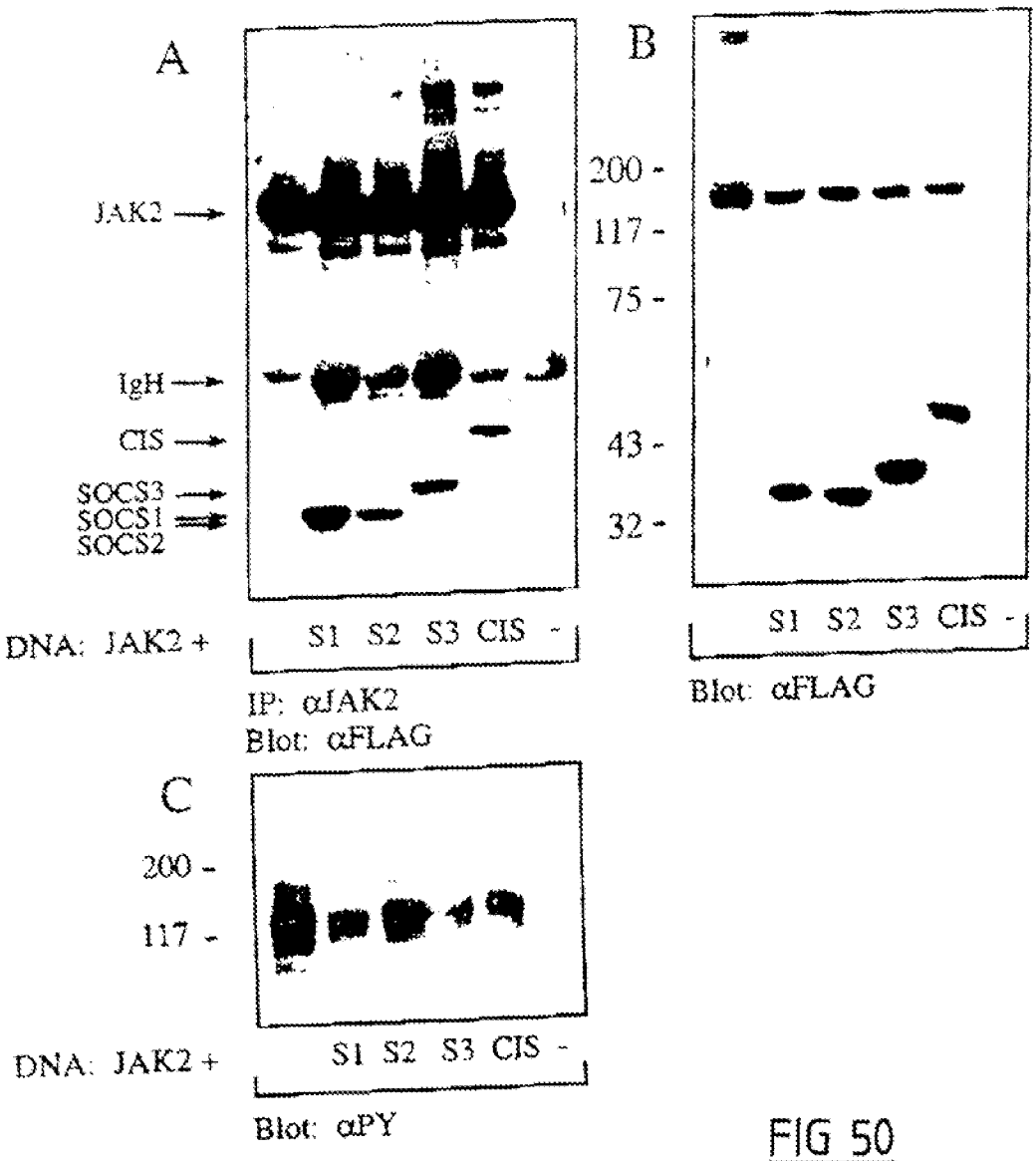

A
JAK2
IgH
CIS
SOCS3
SOCS1
SOCS2
DNA: JAK2 +
S1 S2 S3 CIS -
IP: αJAK2
Blot: αFLAG
B
200 -
117 -
75 -
43 -
32 -
S1 S2 S3 CIS -
Blot: αFLAG
C
200 -
117 -
DNA: JAK2 +
S1 S2 S3 CIS -
Blot: αPY

FIG 50

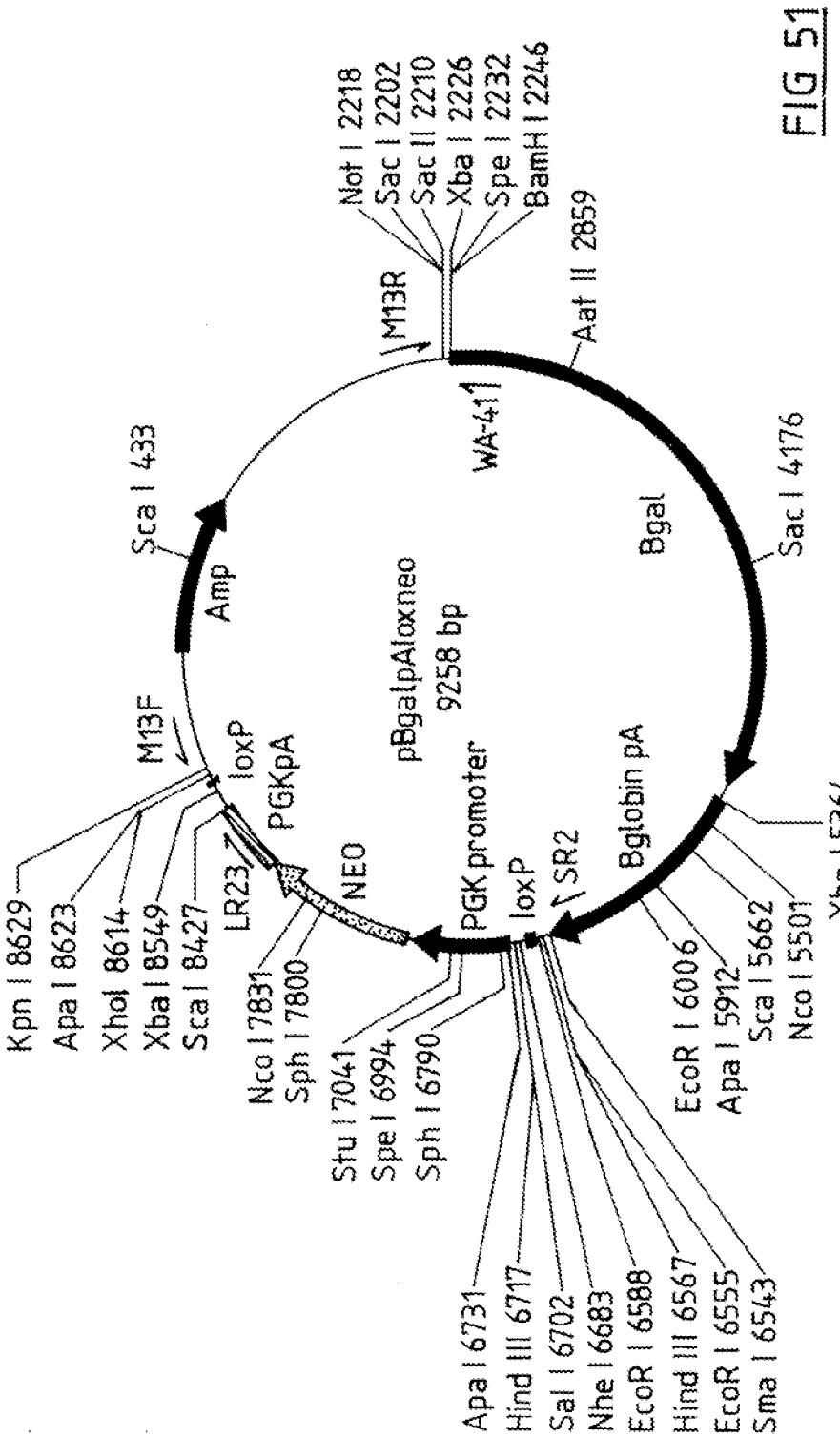
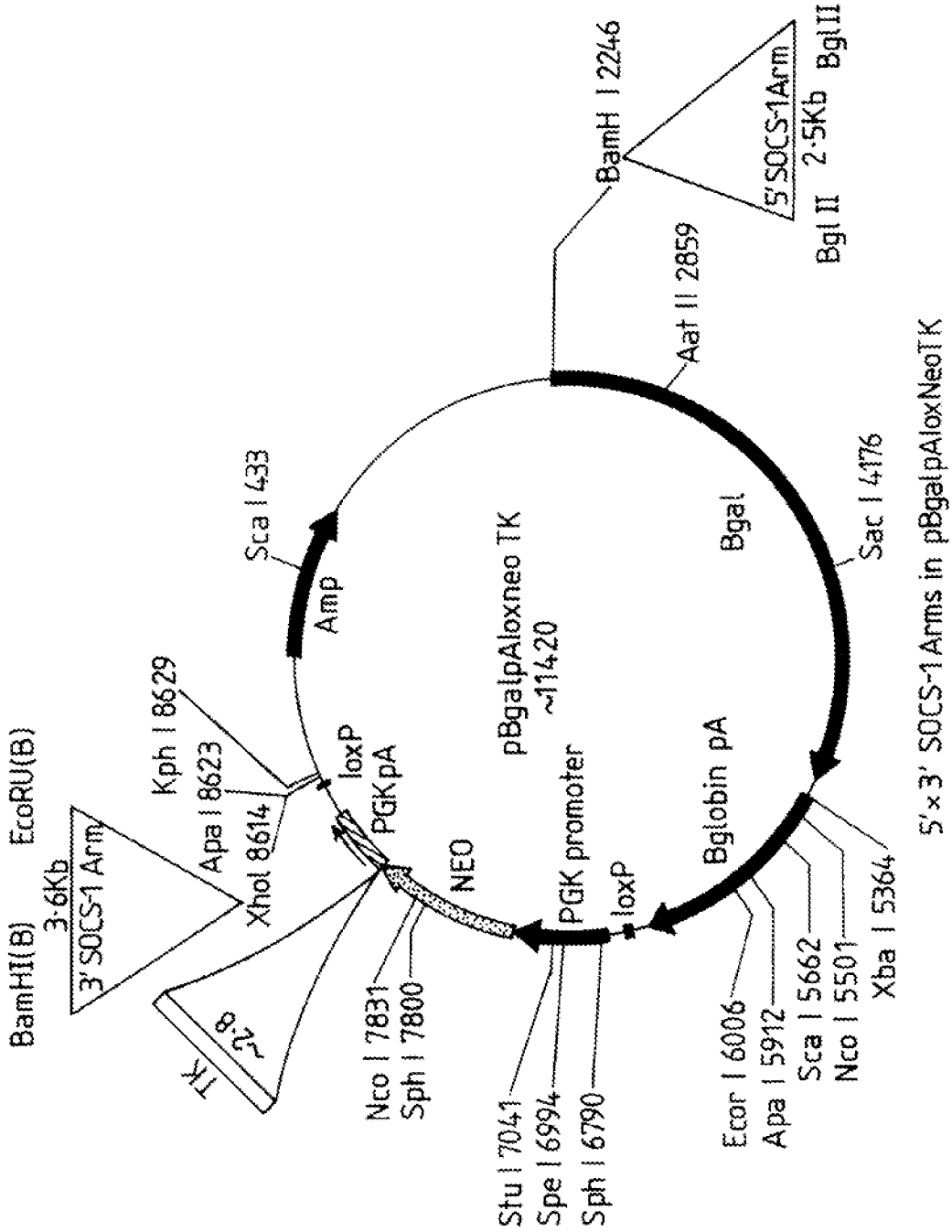

pBgalpAloxneo
9258 bp
Bgal
Amp
WA-411
M13R
M13F
loxP
PGKpA
NEO
PGK promoter
loxP
SR2
Bglobin pA
Not I 2218
Sac I 2202
Sac II 2210
Xba I 2226
Spe I 2232
BamH I 2246
Aat II 2859
Sac I 4176
Xba I 5364
Nco I 5501
Sca I 5662
Apa I 5912
EcoR I 6006
Sca I 433
Kpn I 8629
Apa I 8623
Xhol 8614
Xba I 8549
Sca I 8427
LR23
Nco I 7831
Sph I 7800
Stu I 7041
Spe I 6994
Sph I 6790
Apa I 6731
Hind III 6717
Sal I 6702
Nhe I 6683
EcoR I 6588
Hind III 6567
EcoR I 6555
Sma I 6543

FIG 51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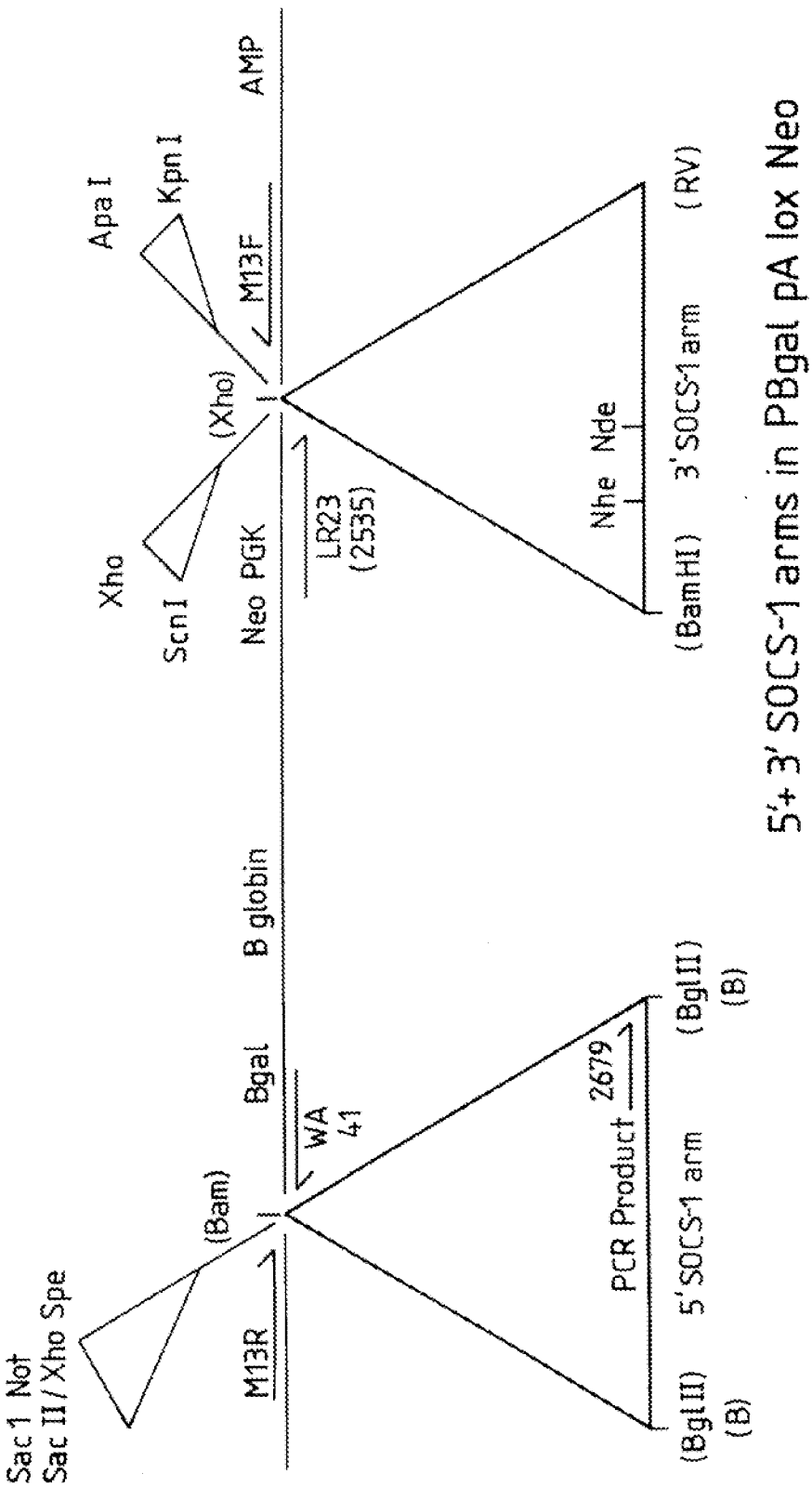
EcoRU(B)
3·6Kb
3' SOCS-1 Arm
Kph I 8629
Apa I 8623
XhoI 8614
TK
2·2Kb
Sca I 433
Amp
loxP
PGK pA
NEO
pBgalpAloxneo TK
~11420
PGK promoter
loxP
Bglobin pA
Bgal
Aat II 2859
BamH I 2246
5'SOCS-1Arm
2·5Kb
Bgl II
BglII
Sac I 4176
5'×3' SOCS-1 Arms in pBgalpAloxNeoTK
Nco I 7831
Sph I 7800
Stu I 7041
Spe I 6994
Sph I 6790
Ecor I 6006
Apa I 5912
Sca I 5662
Nco I 5501
Xba I 5364

FIG 52

FIG 53 SOCS-1 Knockout Construct



INTERNATIONAL SEARCH REPORT

International Application No.
PCT/AU 97/00729

A. CLASSIFICATION OF SUBJECT MATTER

Int Cl[6]: C07K 2/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
STN Peptide sub sequence search
STN [LIVMAP]. [PTS]..[LIVMAP]..[LIVMAF YW] [CTS] [RKH]..[LIVMAP] {3}[LIVMAPGC TS].{1,50}[LIVMAP]..[LIVMAP] P [LIVMAPG] [PN] {1,50} [LIVMAP]..[YF] [LIVMAP]

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X,P	WO 96/39427 (Trustees of Dartmouth College) 12 December 1996 The whole document	1-40
X	Yeast vol 12 No 15 issued 1996 Delaveau, Th et al. "Analysis of a 23 kb region on the left arm of yeast chromosome IV" pages 1587-1592	1-40
X	Science vol 270 No 5234 issued 1995 labeit, Set al "Titins: giant proteins in charge of muscle ultrastructure and elasticity" pages 293-6	1-40

☐ Further documents are listed in the continuation of Box C

☒ See patent family annex

* Special categories of cited documents:

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"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search
20 November 1997

Date of mailing of the international search report
12 DEC 1997

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INTERNATIONAL SEARCH REPORT

International Application No.
PCT/AU 97/00729

C (Continuation) **DOCUMENTS CONSIDERED TO BE RELEVANT**

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	The EMBO Journal Vol 14 No 12 issued 1995 Yoshimura, A et al "A novel cytokine - inducable gene CIS encodes and SH2 - containing protein that binds to tyrosine - phosphorylated interleukin 3 and erythropoietin receptors" pages 2816-26	1-40
X	AU, A, 27924/95 (Flügge, U.I.) 17 August 1995 The whole document, particularly pages 29-32	1-40
X	Biochemistry vol 34 No 8 issued 1995 Weber, A et al "The 2-oxoglutarate/malate translocator of chloroplast envelope membranes:molecular cloning of a transporter containing a 12-helix motif and expression of the functional protein in yeast cells. pages 2621-7	1-40
X	Journal of Bacteriology Vol 176 No 24 issued 1994 Iwai, A et al "Molecular cloning and expression of an isomalto-dextranase gene from Arthrobacter globiformis T6" pages 7730-4.	1-40
X	Nucleic Acids Research Vol 122 No 11 issued 1994 Althoff, S et al "Molecular evolution of SRP cycle components:functional implications" pages 1933-47	1-40
X	Nature vol 368 No 6466 issued 1994 Wilson, R et al "2.2 Mb of contiguous nucleotide sequence from chromosome III of C elegans" pages 32-8.	1-40
X	The EMBO Journal Vol 11 No 5 issued 1992 Labeit, S et al "Towards a molecular understanding of Titin" pages 1711-16	1-40
X	Advances in Biophysics Vol 33 (Muscle Elastic Proteins) issued 1996 Kolmerer, B et al "A systematic search of the data bases for sequences homologous to titin/connectin" pages 3-11	1-40
X	Microbiology Vol 142 no 8 issued 1996 Yoneyama, H "Protein C (OprC) of the outer membrane of Pseudomonas aeruginosa is a copper-regulated channel protein" pages 2137-2144.	1-40
X	Journal of Bacteriology Vol 178 No 15 issued 1996 Limberger, Ret al. "Organisation, transcription and expression 'of the 5' region of the fla operon of Treponema phagedenis and Treponema pallidum" pages 4628-4634.	1-40
X	The Journal of cell biology Vol 133 No 6 issued 1996 Goodson, H. V et al "Synthetic lethality screen identifies a novel yest myosin I gene (MY05): myosin I protein are required for polarisation of the actin cytoskeleton" pages 1277-1291	1-40
X	Genes and Development Vol 9 No 24 issued 1995 Herrscher, R F et al "The immunoglobulin heavy-chain matrix-associating regions are bound by Bright: a B cell-specific trans-activator that describes a new DNA-binding protein family" pages 3067-82	1-40

INTERNATIONAL SEARCH REPORT
Information on patent family members

International Application No.
PCT/AU 97/00729

This Annex lists the known "A" publication level patent family members relating to the patent documents cited in the above-mentioned international search report. The Australian Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

Patent Document Cited in Search Report		Patent Family Member					
AU, A	27924/95	CA	2192849	DE	4420782	EP	765393
		HY	9603441	WO	95/34654		

END OF ANNEX